O-Chlorobenzylidene Malononitrile (CS Riot Control Agent) Exposures and Associated Acute Respiratory Illnesses in a United States Army Basic Combat Training Cohort

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-Joe

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Joseph J. Hout

March 14, 2014

ABSTRACT

O-Chlorobenzylidene Malononitrile (CS Riot Control Agent) Exposures and Associated Acute Respiratory Illnesses in a United States Army Basic Combat Training Cohort.

Major Joseph J. Hout, Doctor of Philosophy, 2014

Thesis directed by: LTC Alex Stubner, PhD, Department of Preventive Medicine and Biometrics

BACKGROUND

Acute Respiratory Illnesses (ARIs) are among the leading causes for hospital visits and lost work time in United States (US) military training populations. The occurrence of ARIs in military recruit populations has been well studied, but understanding of casual factors is limited. Studies consistently demonstrate an increased ARI rate during week four through six of US Army Basic Combat Training (BCT), immediately following mandatory exposure to the riot control agent o-chlorobenzylidene malononitrile (CS tear gas) during Mask Confidence Training (MCT). MCT is conducted during the first three weeks of BCT by thermally dispersing CS in a relatively air-tight structure where recruits wearing military issued M40 series protective masks enter, perform a series of exercises, remove their protective masks, and exit the structure. Recruits feel an intense burning sensation on exposed skin and, after removing the mask, almost immediate lacrimation, violent coughing spasms, and sometimes vomiting. Partly as a result of initial studies conducted for this dissertation, the US Army implemented All

Army Activities Message (ALARACT) 051/2013 to decrease CS exposure concentrations and health effects associated with this training. Currently, no studies exist that quantify CS exposure concentrations in a US Army BCT population; furthermore, there are no studies that consider CS exposure as a potential risk factor for ARI diagnoses in this population.

METHODS

This observational prospective cohort study quantified CS exposure concentrations and captured associated ARI health outcomes before and after implementation of ALARACT 051/2013 in over 12,000 individuals attending BCT at Fort Jackson, South Carolina (SC) from August 1, 2012 – April 30, 2013. CS exposure concentrations were determined using Occupational Safety and Health Administration (OSHA) modified National Institute for Occupational Safety and Health (NIOSH) Physical and Chemical Analytical Method (P&CAM) 304; ARI count data was obtained from existing databases populated by training officials and medical staff. CS concentrations were matched to corresponding military unit, exposure group data, and ARI incidence and were used to calculate means, chi-squared values, Breslow-Day tests for interaction, stratified risks, attributable risks (AR), as well as unadjusted and Mantel-Haenszel adjusted risk ratios (RR) with corresponding 95% confidence intervals (95% CI). The Poisson regression analysis was also used to explore the relationship between CS exposure concentrations and ARI outcomes. Known ARI confounders such as building of residence and week of training were captured and included in the analyses.

RESULTS

The pre-ALARACT cohort consisted of 6,723 trainees and seven chamber operators attending BCT at Fort Jackson, SC from 1 August to 25 September 2012. Trainee exposures ranged from 1.74 to 55.24 mg/m^3 ($\overline{x}$=9.9 mg/m^3) and chamber operator exposures ranged from 2.37 to 35.07 mg/m^3 ($\overline{x}$=10.3 mg/m^3). All trainees were potentially exposed to CS concentrations exceeding the American Conference of Industrial Hygienist Threshold Limit Value-Ceiling (TLV-C) (0.39 mg/m^3), 6,589 (98%) of which were potentially exposed to concentrations exceeding the value deemed Immediately Dangerous to Life and Health (IDLH) (2.0 mg/m^3) by the NIOSH. All chamber operators were exposed to concentrations exceeding both the TLV-C and the IDLH. Recruits had a significantly higher risk (RR=2.44, 95% CI=1.74, 3.43) of being diagnosed with ARI following exposure to CS compared to the period of training preceding exposure, and incidence of ARI after CS exposure was dependent upon the CS exposure concentration (p=0.03). There was a significant pre/post exposure ARI difference across all CS concentration levels (p=0.006), however no significant differences were detected among these rate ratios (p=0.72).

The post-ALARACT cohort consisted of 5298 trainees and six chamber operators attending BCT at Fort Jackson, SC from 13 March – 30 April, 2013. A 10-fold reduction (p<0.001) in CS exposure concentrations was observed (pre versus post-ALARACT) with recruit exposures ranging from 0.26 – 2.78 mg/m^3 ($\overline{x}$=1.04 mg/m^3) and chamber operators from 0.05 – 2.22 mg/m^3 ($\overline{x}$=1.05 mg/m^3). The overall risk of being diagnosed with ARI also decreased, but was still significantly higher in the seven days following exposure to CS compared to the seven-day period before the exposure (RR=1.79, 95%CI=1.29, 2.47) resulting in a 26.85% (95%CI=-0.17, 0.54) effectiveness for the

intervention. Post-chamber ARI rates (p=0.02) were still dependent upon CS exposure concentration, and pre/post-chamber ARI rate ratios were significantly elevated at all concentration categories higher than the TLV-C (0.39 mg/m^3).

CONCLUSIONS

This study is the first to quantify CS exposure concentrations and associate them to ARI health outcomes in a US Army BCT population. The majority of the pre-ALARACT cohort was exposed to CS levels requiring a greater level of respiratory and skin protection than afforded at the time of the study. Since CS exposure concentrations exceeded published guidelines and were positively associated with ARI health outcomes in this population, interventions designed to reduce respiratory exposures were recommended to US Army safety officials. These recommendations became the framework of ALARACT 051/2013, which reduced the quantity of CS used during MCT, specified a maximum unmasked time of 15 seconds, and mandated semi-annual industrial hygiene assessments of all US Army mask confidence chambers. The post-ALARACT cohort experienced a significant reduction in CS exposure concentrations accompanied by a decrease in associated ARI health outcomes. Although CS concentrations were approximately 10 times lower than the pre-ALARACT cohort, the results still suggest that ARI diagnosis after CS exposure is positively associated with CS concentration. Despite the success of this intervention in lowering CS concentrations below the IDLH, mean recruit CS concentrations still exceed the ACGIH TLV-C. Efforts should be made to further decrease CS concentrations since this research suggested a decreased ARI risk for CS concentrations below this level.

Future research is needed to better characterize ARI health outcomes reported here by differentiating between CS induced irritation or infection, and to explore these outcomes at CS concentrations below the ACGIH TLV-C. Research is also needed to determine if ALARACT 051/2013 resulted in decreased hospital burden and lost training time in the BCT population.

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CHAPTER 1: Introduction

BACKGROUND

Acute respiratory illnesses (ARIs), which encompass a broad range of febrile and afebrile clinical diagnoses such the common cold, influenza, bronchitis, bronchiolitis, pneumonia and other respiratory ailments, account for over 429 million incident cases per year globally and are the leading cause of disease burden in the world (81). ARI is also a leading cause of health loss in the United States (US) and a significant source of morbidity in US military training populations, accounting for more medical encounters and lost work time than any other illness or injury in US military recruits from 2010 through 2012 (7; 8; 11; 71). Although the occurrence of ARI in this population has been well studied, the understanding of causal factors is limited (13; 33; 47; 71).

In the early 1990's, British Surgeon Lieutenant Commander Pipkin described an ARI outbreak occurring in a military training population in the Royal Marines where cases peaked shortly following exposure to the riot control agent, o-chlorobenzylidene malononitrile (CS) (62). CS exposure results in almost immediate pain and discomfort throughout the respiratory tract and sometimes results in violent coughing spasms, damage to the respiratory epithelium, pulmonary edema, and secondary infection (67; 69; 82). Pipkin speculated that a combination of these effects may have promoted the spread of ARI within the exposed Royal Marines (62). The biological plausibility of this hypothesis is feasible as opportunistic respiratory infections (including those associated with ARI) have been shown to spread via direct and indirect contact and to commonly

occur following chemical irritation or injury (5; 80). Unfortunately, due to a small sample size, Pipkin's hypothesis could not properly be tested.

All US Army soldiers are exposed to CS while completing mandatory mask confidence training (MCT) during basic combat training (BCT). A 2011 study showed that the CS concentration experienced during this training may exceed the American Conference of Industrial Hygienists (ACGIH) threshold limit value ceiling (TLV-C), the National Institute for Occupational Safety and Health (NIOSH) recommended exposure limit ceiling (REL-C) and the concentration deemed immediately dangerous to life and health (IDLH) by NIOSH, causing eye and respiratory irritation as well as damage to the respiratory epithelium (40). Research also showed that both febrile and afebrile ARI rates peaked in a US Army recruit cohort at Fort Jackson, SC during training weeks four to six of BCT; immediately following exposure to CS (80).

Given the potential for high levels of acute CS exposure in Army BCT prior to the observed increase in ARI rates make it temporally plausible that CS exposure could induce damage to the respiratory tract leading to increased susceptibility to ARIs and an increase in ARI incidence. It is also possible that CS-induced expectoration promotes the spread of pathogens responsible for ARIs in this population. Currently, no studies have considered the mandatory exposure to CS or the CS concentrations experienced during the first three weeks of the BCT training cycle as a covariate in their ARI analyses. Additionally, there are no studies published that characterize CS exposures during MCT at US Army BCT.

STUDY OVERVIEW

The goal of this research is to prospectively assess the relationship between occupational exposures to CS and subsequent ARI diagnoses in a recruit population attending US Army BCT to test the following hypotheses of interest:

1) CS is evenly distributed inside a US Army mask confidence chamber.
2) CS exposure concentrations exceed the ACGIH TLV-C during MCT using US Army training guidelines.
3) CS exposure concentrations exceed the NIOSH IDLH during MCT using US Army training guidelines.
4) ARI rates will be higher in the seven days following MCT compared to the seven days preceding exposure at all CS exposure concentrations.
5) ARI rates will increase with increasing CS exposure concentration.
6) Implementation of ALARACT 051/21013 will result in CS exposure concentrations less than the ACGIH TLV-C.
7) Implementation of ALARACT 051/21013 will result in CS exposure concentrations less than the NIOSH IDLH.
8) Implementation of ALARACT 051/21013 will result in decreased ARI rates.

The objectives of this research are to:

1) Determine CS concentrations during US Army MCT.
2) Determine the incidence and distribution of ARI in a US Army BCT recruit population before and after completion of MCT.
3) Link ARI health outcomes to CS exposure data to investigate causality.
4) Assess effectiveness of MCT changes in reducing CS exposure concentrations and ARI rates.

The following specific aims provide the framework necessary to test the hypotheses and accomplish the goal and objectives of this research:

1) Characterize CS dispersion in a mask confidence chamber at Fort Jackson, SC during US Army BCT from Aug 2012 through April 2013.
2) Quantify CS exposure levels for BCT recruits and chamber operators before and after implementation of ALARACT 051/2013 during MCT at Fort Jackson, SC from Aug 2012 through April 2013.
3) Use an observational, prospective cohort study design to capture the incidence and distribution of BCT recruit ARI starting seven days prior to the MCT through seven days after completion at Fort Jackson, SC from August through September 2012 and March through April 2013.
4) Assess and compare the strength of association, temporality, and dose-response between BCT recruit CS exposures and corresponding ARI outcomes occurring from August through September 2012 and March through April 2013 at Fort Jackson, SC.

The study is strictly observational and will neither introduce new exposures nor involve the collection or use of personal or identifying information. Exposure to CS during MCT is a BCT graduation requirement (31). Recruit and chamber operator CS exposure concentrations will be assessed using Occupational Safety and Health Administration (OSHA) modified NIOSH Physical and Chemical Analytical Method (P&CAM) 304 (52; 61). All sampling media will be shipped within 24 hours of collection to a certified laboratory for analysis.

Existing databases populated by training officials and medical staff at Moncrief Army Community Hospital (according to the Fort Jackson acute respiratory disease standard operating procedures) will provide ARI count data (27; 73). All data sets will be de-identified and contain only date specific ARI counts and rates by platoon; no other data fields will be provided to investigators.

Platoon specific ARI rates will be linked to platoon specific chemical exposure data gathered during MCT. Descriptive statistics will be used to generate frequency tables and calculate means where applicable. One way analysis of variance (ANOVA) tests, Chi-squared analyses, Breslow-Day tests for interaction, stratified risks, attributable risks (AR), as well as unadjusted and Mantel-Haenszel adjusted risk ratios (RR) with corresponding 95% confidence intervals (95% CI), and Poisson Regression analyses will be conducted to test the hypotheses of interest.

Three manuscripts will be written based upon this study to address the aforementioned research objectives and hypotheses. The first manuscript will focus on assessing the CS concentrations experienced by both recruits and chamber operators in a US Army mask confidence chamber during MCT and will compare these to established CS exposure guidelines. This manuscript will also discuss the dispersion of CS within the chamber, exposure times (with and without a respiratory equipped), and industrial hygiene controls that can be implemented increase safety for participants. The second manuscript will focus on ARI health outcomes and their relationship to CS exposure and CS exposure concentrations. Known ARI confounding variables such as week of training and building type will be included in the analysis. The third and final manuscript will focus on CS exposure concentrations for recruits and chamber operators and their

relationship to ARI health outcomes after the implementation of All Army Activities Message (ALARACT) 051/2013 that changed MCT procedures across the US Army (75). It will also assess the effectiveness of this intervention in decreasing CS concentrations and associated ARI health outcomes in the Ft. Jackson BCT population.

SIGNIFICANCE

This research will be the first to quantify CS exposures in US Army BCT. If these hypotheses are correct, this research will impact military public health by identifying excessive exposures to CS and will prompt changes in doctrine to reduce CS concentrations during US Army MCT to levels considered safe by the ACGIH and NIOSH. These changes could impact an even larger audience since several entities including civilian law enforcement, foreign militaries, and other branches of the US armed forces frequently train with CS using similar procedures.

The study will also impact military public health by helping to explain the recurring trend in Army BCT ARI rates and could lead to attenuation of the increased ARI rates observed during weeks four through six of BCT. It will be the first study to associate CS exposure to ARI and to document strength of association, temporality and dose-response to support causality. If ARI is positively associated with CS exposure, reducing CS exposure concentrations or limiting exposure could decrease lost training time thus saving thousands of lost man-hours and decreasing the burden on the health care system.

CHAPTER 2: Literature Review

ACUTE RESPIRATORY ILLNESSES (ARI)

Definition

ARI is a broad disease classification that encompasses a multitude of clinical diagnoses including both upper and lower respiratory illnesses, with and without fever (10). In the Fort Jackson BCT population, the term ARI captures the following International Classification of Diseases Version 9 (ICD-9) codes: 079.99 Viral infection, not otherwise specified (NOS); 382.9 Otitis media NOS; 460 Nasopharyngitis, acute; 461.9 Acute sinusitis; 465.8 Acute upper respiratory infections of other multiple sites; 465.9 Acute upper respiratory infections of unspecified site; 466.0 Bronchitis, acute; 486 Pneumonia, organism NOS; 487.0 Influenza with pneumonia; 487.1 Influenza with respiratory manifestation, not elsewhere classified (NEC); 487.8 Influenza with manifestation NEC; 490 Bronchitis NOS; 784.1 Pain, Throat; and 786.2 Cough (73).

Diagnosis

Healthcare facilities see more patient visits for ARI related symptoms than any other acute manifestation (36). A small group of symptoms, including sore throat, cough, runny nose, shortness of breath, headache, tonsillar exudates, or tender cervical lymphadenopathy, are common to most ARIs. This often makes it difficult for the clinician to choose one diagnosis over another in some cases (37).

For example, an acute cough (a common symptom of ARI) is one of the most frequent reasons people seek medical attention (43). The common cold is almost always diagnosed when a patient presents with signs and symptoms of ARI including sneezing,

running nose, excessive tearing, and irritation of the throat regardless of oral temperature. However, these symptoms are also consistent with acute bacterial sinusitis or respiratory irritation due to environmental irritants (44).

Often times, laboratory testing is not conducted due to cost and the self-limiting nature of ARIs. Furthermore, many of those who present with ARI symptoms have no identifiable infective pathogen making the test pointless. For example, in a 2004 prospective study that examined nearly 600 subjects who presented with ARI symptoms, no pathogen could be identified in 49% of patients. Authors attributed the lack of infective etiology in this population to non-infective, irritant induced ARI symptoms (36).

ARI in BCT

Regardless of the cause, ARIs present a significant source of morbidity in US military training populations and historically account for 25-30 percent of infectious disease hospitalizations (34).

In order to be diagnosed with an ARI, a recruit must first request to go to "sick call". The recruit is transported to a Battalion Aide Station (BAS) or to the Troop Medical Clinic (TMC) where they are screened using an algorithm (73). If a recruit has at least one sign or symptom of ARI (e.g. sore throat, cough, runny nose, shortness of breath, headache, tonsillar exudates, or tender cervical lymphadenopathy) but a temperature is less than 100.5^{o}F, the recruit is typically provided with over–the-counter medicine and returned to training. However, if a recruit presents with at least one ARI sign or symptom and a temperature greater than 100.5^{o}F, staff will obtain a throat culture and admit the recruit to medical quarters for at least 24 hours.

All medical encounters (afebrile and febrile) are captured using International Classification of Diseases Version 9 (ICD-9) codes which are stored in the recruit's electronic medical record. These data are used by US Army medical personnel to conduct weekly surveillance of Acute Respiratory Disease (ARD) (synonymous with febrile ARI) at each of the five Army BCT sites (Figure 1) (18; 73). The US Army has conducted routine surveillance for febrile respiratory illnesses since the mid-1960s (15).

Applicable ARI Studies

A study conducted from 1985 to 1994 observed 65,184 febrile ARI hospitalizations in a US Army recruit population with a crude hospitalization rate of 0.45 per 100 trainees per week (15). Most cases occurred within the first few weeks of training, with nearly 20 percent testing positive for Group A beta hemolytic Streptococci (GABHS).

Another study in 2002 found that over 90% of recruits experienced respiratory symptoms during an 8-week BCT cycle at Fort Jackson, SC. Respiratory related hospitalizations peaked during weeks four and five, while self-reported febrile illnesses peaked during week three. Investigators attributed the rise in ARI rates to lack of an effective adenovirus immunization program (47).

A similar study was conducted in 2004 to investigate the effect of building design on ARI rates in a BCT population at Fort Jackson, SC. ARI rates here followed a similar pattern as previously discussed; peaking for both febrile and afebrile ARI during weeks four through six of the training cycle. Investigators concluded that the week of training was significant at almost all levels, across genders, and ARI outcomes. They attributed this to exposure to viruses or bacteria early in the training cycle followed by increased

immunity as the training cycle progressed combined with the effects of the training itself (80).

Recent surveillance efforts conducted by the Armed Forces Health Surveillance Center (AFHSC) suggest that ARIs accounted for more medical encounters and lost work time than any other illness or injury in US military recruits from 2010 through 2012 (7; 8; 11; 71). However, the resumption of Adenovirus four and seven vaccines to all new recruits in late 2011 resulted in a significant decrease in febrile ARI in the months following reintroduction (35).

A follow-on study also suggested a vaccine-related reduction in ARI rates in recruits who entered service after implementation of the vaccines (10). In BCT at Fort Jackson, SC, the adenovirus rate dropped from 2.40 cases per 100 training weeks to 0.00 cases per 100 training weeks only 4 months after implementation (51).

FORT JACKSON BASIC COMBAT TRAINING

Population

Fort Jackson, SC is the largest BCT site in the US Army and is responsible for training more than fifty percent of all recruits (approximately 40,000 personnel/year) and sixty percent of all females that enter the US Army each year. All training is gender-integrated; only latrines and sleeping areas are gender separated. During fiscal year 2013, 56.6 percent of recruits were Caucasian; 22.8 percent were African American; 14.8 percent were Hispanic; and 5.8 percent were classified as other race (76).

Since BCT gathers recruits from a widely varied geographic distribution, it creates an environment where exposure to pathogens that recruits are immunologically susceptible to is amplified. This, combined with sleeping and training in close proximity

to others accompanied by the stress associated with military training, increase the risk for acute respiratory illnesses in this population (10). With this in mind, all recruits are vaccinated against influenza, measles, rubella, polio, tetanus, diphtheria, meningococcal diseases and adenovirus four and seven upon arrival to BCT (34; 35).

Housing

Recruits are assigned to one of two training brigades located on Fort Jackson; 165th Infantry Brigade or the 193rd Infantry Brigade. Each training brigade consists of four to five training battalions; and, each battalion consists of four to five companies. Each company has four platoons that are composed of approximately 50 recruits.

Recruits reside in one of four basic types of barracks: 1) Starship barracks (SS) – Fixed facilities consisting of 60 person rooms; 2) Relocatable barracks (RL) – Movable facilities that can accommodate up to 50 soldiers per room; 3) Rolling Pin barracks (RP**)** **–** Fixed facilities consisting of eight-person rooms; or 4) Star base barracks (SB) – Newer housing units with multiple 60-person rooms.

Studies have shown that the barracks in which a recruit lives is associated with clinical diagnoses of both febrile and afebrile ARI in this population with risks significantly higher in barracks where recruits sleep together in 60 person rooms compared to eight person rooms (80).

Training

BCT is conducted over a 10-week period using a red, white and blue phased system. The red phase takes place during the first three weeks of BCT and consists of total control where recruits begin their integration into Army life. Recruits learn the Army values and Warrior Ethos, develop basic combat skills, and improve their physical

endurance. This is followed by the white phase during weeks four through six of BCT. This phase focuses primarily on development of combat skills to include weapons qualification. Weeks seven through ten make up the blue phase, which focuses on tactical training, team building, and self-discipline. This phase culminates with a field training exercise designed to test recruit proficiency in warrior tasks and unit level combat operations (31).

Studies show that a recruit's week of training is associated with diagnosis of febrile and afebrile ARI in this population. These rates historically peak during week four through six of BCT, then decline back to baseline by the end of BCT (47; 80). Several theories have been developed to explain this disease pattern including exposure to previously unencountered pathogens followed by development of immunity later in the BCT cycle and decreased immune function early in the BCT cycle due to stress and the rigors of military training (80). One such training event that could potentially influence ARI rates is mandatory exposure to the riot control agent o-chlorobenzylidene malononitrile during the red training phase.

O-CHLOROBENZYLIDENE MALONONITRILE (CS RIOT CONTROL AGENT)

Origin

In the late 1920s, Ben Corson and Roger Stoughton at Middlebury College, Vermont reacted 2-chlorobenzaldehyde with malononitrile in the presence of piperidene to create o-chlorobenzylidene malononitrile (16). They immediately recognized that CS was unlike the other compounds in their study as it produced a sneezing effect and caused a burning sensation on exposed skin. It was not until the late 1950s however, that CS was developed as a riot control agent (RCA) when it was found that CS produced

incapacitating effects at lower concentrations than chloroacetophenone (CN). In 1959, CS replaced CN as the standard RCA in the US and is currently the most widely used RCA in the world.

Properties

Despite the frequent use of the term CS tear gas, CS is not a gas; rather it is a solid at room temperature. It has a relatively high molar mass (188.6 grams per mole) owing mostly to chlorine and cyanide constituents (Figure 2) (64). It is only slightly soluble in water but readily dissolves in many organic solvents including acetone, dichloromethane, and benzene. CS melts at 95^{o}C, boils at 310^{o}C and has a vapor density of 6.50 at 20^{o}C making it "heavier" than air when vaporized (3).

CS has a profound effect upon the human body, causing almost immediate eye, skin, and respiratory tract effects. CS causes instant burning and irritation to the eyes, profuse tearing, and uncontrollable blinking at airborne concentrations as low as 0.004 mg/m^{3}(56). Exposed skin is irritated, often turns red, and sometimes blisters. These effects are amplified at increased temperature, humidity, and CS concentrations. CS causes irritation and burning in the nose and mouth accompanied by excessive nasal discharge and mucous production at airborne concentrations as low as 0.023 mg/m^{3}(56). It causes pain and discomfort throughout the respiratory tract and sometimes results in violent coughing spasms, damage to the respiratory epithelium, and pulmonary edema (3; 56; 67; 69).

Common Uses

CS is not considered a chemical warfare agent by the US and can be used during warfare operations; however, such an action requires presidential approval (45). CS is

more commonly used by military and law enforcement agencies for training and riot control operations (56). For example, all new recruits entering the US Army are exposed to CS while participating in Chemical, Biological, Radiological and Nuclear (CBRN) MCT.

Mask confidence training takes place during the first three weeks of BCT. The MCT requires recruits to enter an enclosed, CS-rich environment created by thermally dispersing CS capsules (Department of Defense Identification Code [DODIC] K765) in a relatively air-tight structure (30). The chamber operator builds an initial CS concentration by thermally dispersing one 650 mg CS capsule on the surface of an empty, heated coffee can for every 30 m^3 of chamber volume (19; 22; 38). Once the initial concentration is established, participants enter the chamber wearing a respirator, conduct a series of physical exercises, break and reseal the air-tight seal between their respirators and remove their masks before exiting chamber. Chamber operators remain inside the chamber for the duration of the exercise maintaining the CS concentration by dispersing an additional capsule for every 10 soldiers that pass through the chamber (19; 26; 30; 40). Participants experience an intense burning sensation on exposed skin and, after removing the mask, almost immediate lacrimation, coughing, and sometimes vomiting. Absence of symptoms prior to mask removal develops confidence in the ability of the respirator to protect the user from airborne chemical agents (19; 26).

Exposure Guidelines

Exposure guidelines have been established by various agencies to protect humans from health effects associated with exposure to CS. US Army doctrine dictates the exposure standards set forth by the OSHA will be adhered to unless the exposure

standards set by the ACGIH are more protective; the ACGIH TLV-C, the OSHA PEL and the NIOSH IDLH are applicable to CS exposures (24). The ACGIH TLV-C (0.39 mg/m^3) is a value that should not be exceeded during any part of the exposure scenario and was established to minimize CS-induced damage to the respiratory epithelium and protect against symptoms including burning of exposed skin and potential skin sensitization (3; 4). The OSHA PEL (0.4 mg/m^3) is the average concentration exposure during an eight-hour work period that should not be exceeded during a 40-hour work week and was developed to reduce the risk associated with skin, eye, and respiratory effects (2; 59; 61). The NIOSH IDLH (2.0 mg/m^3) was established to prevent delayed or permanent health effects (including death) associated with exposure and to protect against eye, respiratory, and other effects that could prevent escape from the exposure scenario (53).

Quantification Methods

Upon heating, CS forms a vapor that condenses into an aerosol making it necessary to capture both the gaseous and particulate phases of CS for proper analysis (40). NIOSH Physical and Chemical Analytical Method (P&CAM) 304 uses a 37mm polytetrafluoroethylene (PTFE) filter followed by an in-line Tenax TA sorbent tube to capture both of these phases (52). This method requires a volume of 90 liters of air to be pulled across these media at a flow rate of 1.5 liters per minute for 60 minutes of total sampling time.

Alternate methods for sample collection have emerged since the publishing of NIOSH P&CAM 304. In particular, the OSHA created a modified NIOSH P&CAM 304 method that simplifies sampling and allows for shorter sampling periods (60). This

method uses an OSHA Versatile Sampler (OVS) (Figure 3) tube in lieu of the NIOSH required 37mm PTFE with an in-line Tenax TA sorbent tube (52). The OVS combines a glass filter with a two-section sorbent bed (140/70 Tenax) in one tube to capture both the aerosol and vapor phases of CS (68).

Regardless of collection method, CS is extracted from the media using 20% methylene chloride in hexane and analyzed using High-Performance Liquid Chromatography (HPLC). Alternative analysis methods have been developed using gas chromatography coupled to an electron capture detector (GC/ECD) which provide lower detection limits than HPLC (40). Detection limits have been reported as low as 0.02 ug/m^3 using this technology.

Applicable Studies

In 2001, the US Army Safety Center requested an investigation of two heart failure deaths that occurred just hours after participating in MCT at Fort Knox, KY. The MCT scenario was recreated using published guidelines with no trainees in the chamber. Two air samples were collected and analyzed for CS using NIOSH P&CAM 304 and an additional three samples were collected and analyzed for cyanide and hydrogen cyanide. CS levels were observed as high as 9.76 mg/m^3 (nearly five times IDLH) but cyanide and hydrogen cyanide levels were less than 1.00 ug/m^3. Although an Army investigation determined that the deaths were not attributable to CS exposure, recommendations were made to decrease CS levels during MCT and to use a heat source such as a candle or Sterno canister to decrease the temperature of dispersion (79).

A 2002 study reported nine marines who were hospitalized with a transient pulmonary syndrome shortly after being exposed to CS delivered via thermal grenade

during a training event. Clinical findings were consistent with mild acute lung injury with pulmonary edema. The exposure scenario was recreated and CS concentrations were observed as high as 17.00 mg/m^3 (nearly nine times IDLH). A dose-response effect was suggested as Marines standing in the higher concentration zones were those who required care (69).

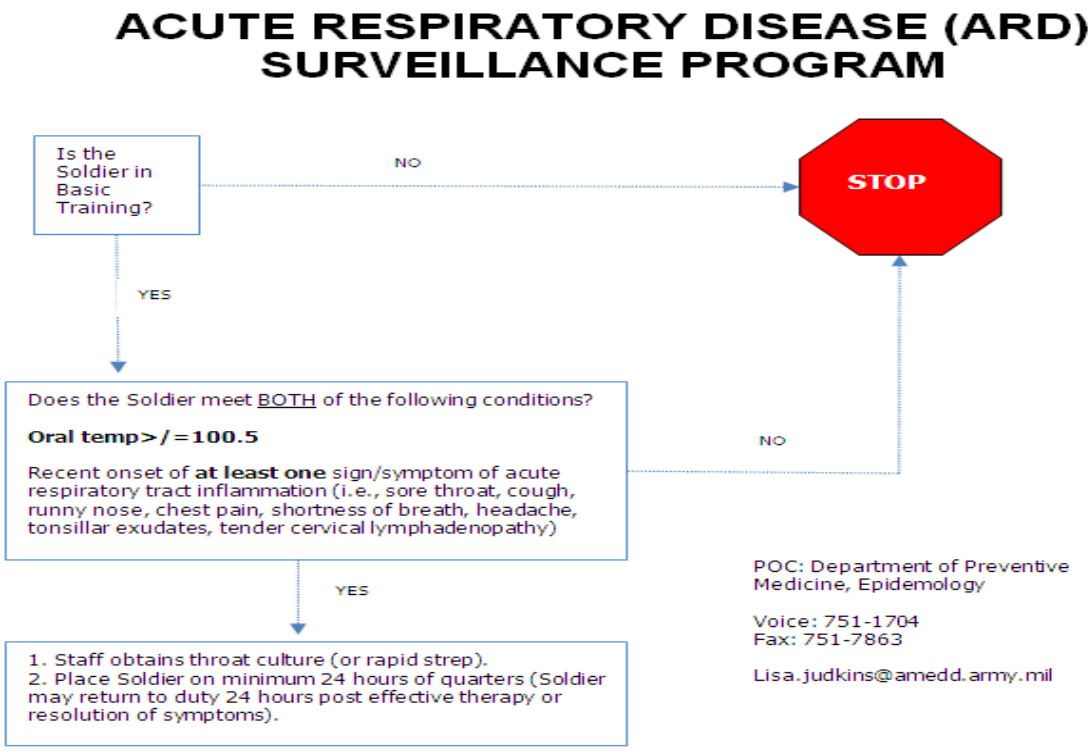
This marine exposure drove research that explored the creation of CS-derived thermal degradation products produced by CS thermal grenades. Kluchinsky *et al.* observed dispersal temperatures greater than 300^{o}C and generation of at least 23 thermal degradation products, some of which may be hazardous to human health (46). However, CS grenades are for outdoor use, have high dispersal temperatures (>600°C), and are not used during MCT (56).

A later study was conducted at the Uniformed Services University of the Health Sciences (USU) to investigate the generation of thermal degradation products produced during MCT by low temperature (<300°C) dispersal of encapsulated CS. CS was dispersed according to US Army guidelines in an unoccupied mask confidence chamber and in a temperature-controlled tube furnace. At least 17 thermal degradation products, some of which were hazardous to human health, were observed (38).

A follow-on study conducted in an unoccupied mask confidence chamber showed CS dispersed in accordance with US Army MCT guidelines resulted in CS concentrations that exceeded the ACGIH TLV-C, the NIOSH REL-C, and NIOSH IDLH. Investigators recommended changes to MCT procedures to prevent over-exposures to CS (40).

Studies cited here illustrate the potential for exposures to CS thermal degradation products and high levels of CS in an Army mask confidence chamber; however, it is

important to note that none of these studies were conducted during live MCT and thus did not represent a population exposure. Furthermore, none of these studies considered the potential link between exposure to CS and subsequent diagnoses of ARI.



Protocol for Environmental Health Fort Jackson Acute Respiratory Disease Surveillance Program, Standing Operating Procedure (SOP), Feb 2012

Figure 1. Algorithm for ARD diagnosis.

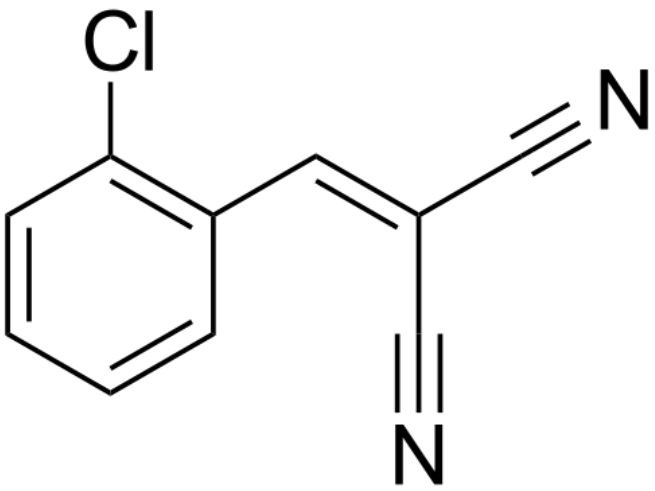


Figure 2. Molecular structure of CS.

Figure 3. OSHA Versatile Sampler.

CHAPTER 3: Methodology

RESEARCH GOAL

The overarching goal of this research is to prospectively assess the relationship between occupational exposures to CS and subsequent ARI diagnoses in a recruit population attending US Army BCT.

HYPOTHESES

The potential for high levels of acute CS exposure in Army BCT prior to the observed increase in ARI rates make it temporally plausible that CS exposure could induce damage to the respiratory tract leading to increased susceptibility to ARIs and an increase in ARI incidence. It is also possible that CS induced mucous production accompanied by decreased mucociliary escalation increases ARI susceptibility and that CS-induced expectoration promotes the spread of pathogens responsible for ARIs in this population. This study will test the following hypotheses of interest:

1) CS is evenly distributed inside a US Army mask confidence chamber.
2) CS exposure concentrations exceed the ACGIH TLV-C during MCT using US Army training guidelines.
3) CS exposure concentrations exceed the NIOSH IDLH during MCT using US Army training guidelines.
4) ARI rates will be higher in the seven days following MCT compared to the seven days preceding exposure at all CS exposure concentrations.
5) ARI rates will increase with increasing CS exposure concentration.

6) Implementation of ALARACT 051/21013 will result in CS exposure concentrations less than the ACGIH TLV-C.
7) Implementation of ALARACT 051/21013 will result in CS exposure concentrations less than the NIOSH IDLH.
8) Implementation of ALARACT 051/21013 will result in decreased ARI rates.

RESEARCH OBJECTIVES

The objectives of this research are to:

1) Determine CS concentrations during US Army MCT.
2) Determine the incidence and distribution of ARI in a US Army BCT recruit population before and after completion of MCT.
3) Link ARI health outcomes to CS exposure data to investigate causality.
4) Assess effectiveness of MCT changes in reducing CS exposure concentrations and ARI rates.

SPECIFIC AIMS

The following specific aims provide the framework necessary to test the hypotheses and accomplish the goal and objectives of this research:

1) Characterize CS dispersion in a mask confidence chamber at Fort Jackson, SC during US Army BCT from August 2012 through April 2013.
2) Quantify CS exposure levels for BCT recruits and chamber operators before and after implementation of ALARACT 051/2013 during MCT at Fort Jackson, SC from August 2012 through April 2013.
3) Use an observational, prospective cohort study design to capture the incidence and distribution of BCT recruit ARI starting seven days prior to the MCT

through seven days after completion at Fort Jackson, SC from August through September 2012 and March through April 2013.

4) Assess and compare the strength of association, temporality, and dose-response between BCT recruit CS exposures and corresponding ARI outcomes occurring from August through September 2012 and March through April 2013 at Fort Jackson, SC.

STUDY POPULATION

The populations of interest are two gender-integrated cohorts of US Army recruits attending BCT at Fort Jackson, SC. The first cohort attended BCT before implementation of ALARACT 051/2013, from August – September 2012; the second cohort attended after implementation of ALARACT 051/2013, from and March – April 2014.

Army BCT units, designated as approximately 200-person "Companies", scheduled for the MCT were identified by Unit Identification Code (UIC) through coordination with staff at the Chemical, Biological, Radiological, and Nuclear (CBRN) training range. Data on the type of barracks and training week were captured from administrative records provided by Fort Jackson training officials.

Upon arrival to the training site, training units were divided into four ad hoc exposure groups consisting of approximately 50 personnel to proceed through the mask confidence chamber. Exposure group assignment, composition, and size were determined by training officials and were not influenced by investigators. Trainees who completed the MCT with their assigned training unit were enrolled in the cohort; absent

soldiers or those who completed the training but were from a different training unit were excluded.

Officials from each training unit used a personnel roster to document trainee attendance, exposure group (1-4), and completion of the chamber exercise. Count data specifying the number of trainees that completed the chamber exercise and the number of trainees in each exposure group was provided to the investigators after each training event.

CHAMBER CHARACTERIZATION

CBRN staff pre-heated an inverted metal container on an electric hot plate in the center of the chamber (mean temperature = 199.0°C). After approximately five minutes, CS capsules were opened and poured directly into the can causing almost immediate CS dispersion and complete aerosolization in less than three minutes. The first exposure group then entered the mask confidence chamber, lined up against the walls, performed various exercises specified by training staff, and finally removed their protective masks before exiting the chamber. CBRN staff then opened additional CS capsules and poured the contents in the metal container to replace aerosolized CS that may have escaped through the open doors or on recruit uniforms. The next group entered and training continued in this manner until the entire BCT company completed MCT.

Initial sampling was focused CS dispersal within the chamber to determine the number and placement of sampling devices required for exposure assessment. Sampling was restricted to the low traffic area which traversed the chamber from the entrances to the exits. Sampling locations were selected to minimize training interference, provide

representative respiratory exposure locations, and allow access to sampling media for rapid exchange. Four initial sampling locations were chosen based upon these criteria.

The OSHA modified NIOSH P&CAM 304 was used to sample for CS (60). Sampling trains consisted of a 1.4 m section of Tygon tubing connected to OVS tube covers (SKC Inc., Eighty Four, PA) with OVS samplers (SKC Inc., Eighty Four, PA) inserted. Sampling trains were then connected to Aircheck XR5000 Pumps (SKC Inc., Eighty Four, PA) calibrated to 1.5 liters per minute using a BIOS DryCal (Mesa Labs Inc., CO).

OVS samplers were suspended 1.37 m above the floor on sampling stands (SKC Inc., Eight Four, PA) at the four preselected locations to represent human breathing zone exposures. Pumps were sequentially started when an exposure group entered the chamber and sequentially paused after the exposure group exited. OVS tubes were removed, capped, sealed in individual 0.5 L plastic bags, and placed outside the chamber in an ice filled cooler. A new OVS tube was then placed in each sampling train and sampling continued as previously described until all exposure groups completed training. Post sampling flow rates were documented following each sampling event. OVS tubes were packed in ice and shipped within 24 hours via overnight mail to a certified laboratory for analysis. Sample size calculation results required 48 samples (12 from each location) to detect a 0.50 mg/m^3 difference between the sampling locations with 80% power at the 95% confidence level.

EXPOSURE ASSESSMENT

Personal monitoring of trainees was not conducted due to potential training disruption. Thus, area-based, static sampling provided estimated trainee exposure

concentrations. The chamber characterization showed a single static sample located 26 feet from the entrance located in the center of this particular chamber could characterize CS concentration during mask confidence training and be used as a surrogate for individual CS exposure. Sampling methodology was consistent with that used during chamber characterization.

In addition to static sampling, chamber operators were personally monitored using the same sampling train and flow rate as described above. The OVS media was clipped within six inches of the operator's nose and the pump was started when the operator entered the chamber. The pump was stopped only after the entire 200 recruit training unit completed training and the operator departed the chamber. Total sampling time was annotated and samples were capped, sealed in individual bags, packaged on ice with daily area monitoring samples, and shipped within 24 hours to a certified laboratory for analysis.

Recruit exposure groups in the pre-ALARACT cohort were categorized in one of four exposure categories: 0.00-2.00 mg/m^3, 2.01-5.00 mg/m^3, 5.01-10.00 mg/m^3, and greater than 10.00 mg/m^3 based on the IDLH value (2.00 mg/m^3) and the incapacitating range (5.00 – 10.00 mg/m^3) outlined in US Army manuals (23; 53). Exposure categories were assigned for the post-ALARACT cohort as follows: 0-0.39 mg/m^3, 0.40-1.00 mg/m^3, 1.01-1.50 mg/m^3, and greater than 1.50 mg/m^3. Exposure categories were based on ACGIH TLV-C[skin] (0.39 mg/m^3), one-half IDLH (1.00 mg/m^3) and three-fourths IDLH (1.50 mg/m^3) (4; 53).

HEALTH OUTCOME ASSESSMENT

Clinically diagnosed and documented inpatient and outpatient ARIs (both febrile and afebrile) were the outcomes of interest. Medical staff queried the Composite Healthcare Computer System (CHCS) for ARI encounters within companies that completed the MCT using the following International Classification of Diseases Version 9 (ICD-9) codes: 079.99 Viral infection, not otherwise specified (NOS); 382.9 Otitis media NOS; 460 Nasopharyngitis, acute; 461.9 Acute sinusitis; 465.8 Acute upper respiratory infections of other multiple sites; 465.9 Acute upper respiratory infections of unspecified site; 466.0 Bronchitis, acute; 486 Pneumonia, organism NOS; 487.0 Influenza with pneumonia; 487.1 Influenza with respiratory manifestation, not elsewhere classified (NEC); 487.8 Influenza with manifestation NEC; 490 Bronchitis NOS; 784.1 Pain, Throat; and 786.2 Cough.

Surveillance count data by training unit was provided by local preventive medicine personnel as part of the existing Acute Respiratory Disease (ARD) surveillance program (27). No personal identifying information was provided to the investigators. The surveillance period began seven days prior to CS exposure and ended seven days after exposure (including the day of the exposure). Occurrence of one or more of the ARI related ICD-9 codes as the primary or secondary diagnosis in a trainee's electronic medical record during the surveillance period was designated as a case. This case definition captured both febrile and afebrile ARI cases. Febrile ARI cases had oral temperature of 100.5 F or higher and at least one sign or symptom of acute respiratory tract inflammation (i.e. sore throat, cough, runny nose, chest pain, shortness of breath, headache, tonsillar exudates or tender cervical lymphadenopathy) (27). All cases not meeting this definition were categorized as afebrile. Cases were further divided into pre

and post-chamber ARI cases. A pre-chamber ARI case was defined as occurring with a training unit in the seven day period prior to CS exposure. A post-chamber ARI case was a case that occurred during the seven day surveillance period beginning with exposure to CS in the mask confidence chamber.

To prevent counting multiple encounters by an individual and ensure the most severe health outcomes were captured, first diagnosis of ARI during the surveillance period was used to establish pre or post chamber ARI status. However, if a later febrile ARI diagnosis occurred, it took priority and was used to establish pre or post-chamber ARI case status. Those designated as pre-chamber cases were treated as non-susceptible for post-chamber ARI risk calculations. Cases were cross-referenced with training rosters to determine their cohort and exposure group status. Local preventive medicine personnel provided case counts by training unit, febrile/afebrile, exposure group, and date of encounter.

DATA ANALYSIS

CS concentrations were matched to corresponding BCT units, exposure group data, and ARI incidence and entered into Statistical Package for the Social Sciences (SPSS) for Windows (Version 19, IBM Corp., 2010) for data management. SPSS was used to calculate means, standard deviations, 95% confidence intervals, Shapiro-Wilk tests for normality, and Kruskal-Wallis ANOVA tests for CS concentrations (48; 65). Open Source Epidemiologic Statistics for Public Health (Version 3.01, www.openepi.com., 2013) was used to calculate chi-squared values, Breslow-Day tests for interaction, stratified risks, attributable risks, as well as unadjusted and Mantel-Haenszel adjusted risk ratios (RR) with corresponding 95% confidence intervals (95%

CI). SPSS was also used to conduct Poisson regression analyses to explore the relationship between CS exposure concentrations and ARI outcomes (42).

CHAPTER 4: O-Chlorobenzylidene Malononitrile (CS Riot Control Agent) Exposures in a US Army Basic Combat Training Cohort

ABSTRACT

All US Army soldiers participate in Mask Confidence Training during initial military training and periodically throughout their careers. Training is conducted by dispersing the riot control agent, o-chlorobenzylidene malononitrile (CS) in a relatively air-tight structure where soldiers enter and conduct a series of exercises that culminate with mask removal. This enables participants to experience the incapacitating effects of CS while developing confidence in the mask's ability to protect against airborne chemical warfare agents. This study quantified CS concentrations experienced by 6,723 trainees and seven chamber operators during US Army Basic Combat Training at Fort Jackson, South Carolina from 1 August to 25 September 2012. Trainee exposures ranged from 1.74 to 55.24 mg/m^3 ($\overline{x}$=9.9 mg/m^3) and chamber operator exposures ranged from 2.37 to 35.07 mg/m^3 ($\overline{x}$=10.3 mg/m^3). All 6,723 trainees were potentially exposed to CS concentrations exceeding the American Conference of Industrial Hygienist Threshold Limit Value-Ceiling (TLV-C) (0.39 mg/m^3), 6,589 of which were potentially exposed to concentrations exceeding the value deemed Immediately Dangerous to Life and Health (IDLH) (2.0 mg/m^3) by the National Institute for Occupational Safety and Health. All chamber operators were exposed to concentrations exceeding both the TLV-C and the IDLH.

INTRODUCTION

O-chlorobenzylidene malononitrile (CS), commonly referred to as "tear gas," is an incapacitating agent used by military and law enforcement communities for training and riot control operations (38). The incapacitating effects of CS are well documented

(6; 12; 63; 64; 67; 69). The United States (US) Army exploits these effects to provide realism to combat training events, to validate the serviceability of chemical protective equipment, and to demonstrate protection afforded by the chemical protective mask when challenged by airborne chemical agents (23; 30). All new recruits entering the US Army are exposed to CS during the first month of Basic Combat Training (BCT) while participating in Chemical, Biological, Radiological and Nuclear (CBRN) Mask Confidence Training (MCT). Completion of the mask confidence chamber is a graduation requirement (31). In addition, all US Army soldiers issued a protective mask must complete MCT on an annual basis (28; 30). These two factors make CS a common exposure for many of the nearly 550,000 soldiers serving in the US Army (17).

The MCT requires participants to enter an enclosed, CS-rich environment created by thermally dispersing CS capsules (Department of Defense Identification Code [DODIC] K765) in a relatively air-tight structure (30). Dispersal is controlled by a chamber operator wearing a qualitatively fit-tested M40 series military protective mask equipped with a C2A1 canister. The M40 is a full-face air purifying respirator (APR) that is specifically designed to protect the eyes, face and respiratory tract from airborne chemical warfare agents when used in conjunction with the C2A1 canister (21; 72). The C2A1 canister consists of a high efficiency particulate air (HEPA) filter, followed by an activated carbon filter impregnated with copper, zinc, silver, molybdenum, and triethylenediamine, designed to remove chemical warfare agents and radioactive fallout particles from air entering the mask (49). The chamber operator builds an initial CS concentration by thermally dispersing one 650 mg CS capsule on the surface of an empty, heated coffee can for every 30 m^3 of chamber volume (19; 22; 38). Once the initial

concentration is established, participants enter the chamber wearing the Army Combat Uniform (ACU) (a 50/50 cotton/nylon digital camouflage patterned blouse and trouser worn in conjunction with leather boots that covers the body excluding the hands, wrists, neck and head) and a qualitatively fit–tested M40 with C2A1 canister (74). Trainees conduct a series of physical exercises, break and reseal the air-tight seal between their mask and face, and finally line up in groups of 10 to completely remove their masks before exiting chamber. Chamber operators remain inside the chamber for the duration of the exercise maintaining the CS concentration by dispersing an additional capsule for every 10 soldiers that pass through the chamber (19; 26; 30; 40). Participants experience an intense burning sensation on exposed skin and, after removing the mask, almost immediate lacrimation, coughing, and sometimes vomiting. These events may occur earlier if the mask is defective or improperly fit. Absence of symptoms prior to mask removal develops confidence in the ability of the M40 mask to protect the user from airborne chemical agents (19; 26).

A 2010 study conducted at the Uniformed Services University of the Health Sciences (USU) demonstrated that low temperature dispersal of CS capsules in an unoccupied mask confidence chamber and in a temperature-controlled tube furnace resulted in the formation of at least 17 thermal degradation products, some of which were hazardous to human health (38). A follow-on study conducted in an unoccupied mask confidence chamber showed CS dispersed in accordance with US Army MCT guidelines resulted in CS concentrations exceeding the American Conference of Industrial Hygienist (ACGIH) Threshold Limit Value-Ceiling [skin](TLV-C), the National Institute for Occupational Safety and Health (NIOSH) Recommended Exposure Limit Ceiling (REL-

C), and the level that NIOSH deems Immediately Dangerous to Life and Health (IDLH) (40). These studies illustrate the potential for exposures to CS thermal degradation products and high levels of CS in an Army mask confidence chamber; however they were not conducted during live MCT and thus did not represent a population exposure.

The current observational study quantified CS exposures in a cohort of US Army BCT trainees (n=6,723) and chamber operators (n=7) from 1 August 2012 – 25 September 2012 during BCT at Fort Jackson, SC, and compared them to published exposure guidelines. The study protocol was approved by the US Army Training and Doctrine Command (TRADOC) and the USU Office of Research, and was exempt from the USU Institutional Review Board.

METHODS

The Fort Jackson mask confidence chamber is a 255 m^3 structure used solely for MCT. The chamber has two entrances and three exits at opposing ends of the structure covered by plastic strip curtains to prevent the escape of aerosolized CS (Figure 4). The floor is concrete, walls are cinder block, and the ceiling is painted plywood. Chamber operators establish an initial CS concentration by placing an empty 387-g coffee can on the small burner of a General Electric 1500 Watt Dual Burner Hot Plate (Model# 169214) elevated on a 1.1 m tall table in the center of the chamber (Figure 5). The hot plate is set to high ($\overline{x}$= 199˚C) and the coffee can is preheated for approximately five minutes. Calculations showed that 8.5 capsules were required to establish the initial CS concentration; however chamber operators consistently add 10 CS capsules, agitated and mixed with a stirring rod until all visible CS is aerosolized (approximately five minutes).

Exposure groups ($\overline{x}$=50 trainees) enter the chamber through both entrances, line up against the walls, and conduct a series of exercises that include: breathing normally, breathing deeply, turning head from side-to-side, moving head up and down, rotating chin, running in place for 60 seconds, pulling mask away from the face, clearing the inside of the mask of airborne contaminants, and resealing the mask. Trainees then line up in groups of 10 at two of the exits, remove their protective masks, recite phrases chosen by the instructors, and exit the chamber (Figure 4). Once all trainees in an exposure group exit, a new exposure group immediately enters. One CS capsule is added for every 10 trainees that exit the chamber in the previous exposure group and the training continues as previously described. A maximum of 34 capsules are used for a military company consisting of four exposure groups.

Chamber Characterization

Initial sampling characterized CS dispersal within the chamber to determine the number and placement of sampling devices. Sampling was restricted to the low traffic area which traversed the chamber from the entrances to the exits. Sampling locations were selected to minimize training interference, provide representative respiratory exposure locations, and allow access to sampling media for rapid exchange. As shown in Figure 4, four initial sampling locations are based upon these criteria, three in the mask removal (A-C) area and one near the entrance (D).

The Occupational Safety and Health Administration (OSHA) modified NIOSH Physical and Chemical Analytical Method (P&CAM) 304 was used to sample for CS (60). This method uses an OSHA Versatile Sampler (OVS) tube in lieu of the NIOSH required 37mm polytetrafluoroethylene (PTFE) with an in-line Tenax TA sorbent tube

(52). The OVS sampler combines a glass filter with a two-section sorbent bed (140/70 Tenax) in one tube to capture both the aerosol and vapor phases of CS (68). Sampling trains consisted of a 1.4 m section of Tygon tubing connected to OVS tube covers (SKC Inc., Eighty Four, PA) with OVS samplers (SKC Inc., Eighty Four, PA) inserted. Sampling trains were then connected to Aircheck XR5000 Pumps (SKC Inc., Eighty Four, PA) calibrated to 1.5 liters per minute using a using a BIOS DryCal (Mesa Labs Inc., CO).

OVS samplers were suspended 1.37 m above the floor on sampling stands (SKC Inc., Eight Four, PA) at locations A-D to represent human breathing zone exposures. Pumps were sequentially started when an exposure group entered the chamber and sequentially paused after the exposure group exited. OVS tubes were removed, capped, sealed in individual 0.5 L plastic bags, and placed outside the chamber in an ice filled cooler. A new OVS tube was then placed in each sampling train and sampling continued as previously described until all exposure groups completed training. Post sampling flow rates were documented following each sampling event. OVS tubes were packed in ice and shipped within 24 hours via overnight mail to a certified laboratory for analysis. Sample size calculation results required 48 samples (12 from each location) to detect a 0.50 mg/m^3 difference between the sampling locations with 80% power at the 95% confidence level.

Exposure Assessment

Once the chamber was characterized, the most appropriate locations for CS sampling were determined for characterizing personnel exposures. Personal monitoring of trainees was not conducted due to potential training disruption. It is acceptable

however, to use area samples taken from a fixed location to represent exposures to multiple workers (60). Thus, area-based, static sampling provided estimated trainee exposure concentrations. Sampling methodology was consistent with that used during chamber characterization. Thirty-four military companies comprised of a total of 6,723 trainees were involved in the exposure assessment. Thirty-two of the companies had four exposure groups, while two smaller companies had only three exposure groups. A total of 134 area samples were obtained to represent these exposure groups.

Operators remaining inside the chamber for the duration of the exercise wore personal monitors with a sampling train and flow rate consistent with area monitors. The OVS sampler was clipped to the chamber operator's lapel within 6 inches of the nose; the sampling pump was attached to the operator's belt. The pump was started immediately upon entry into the chamber and was not stopped until the training event was complete and the operator exited the chamber. A total of seven operators were monitored and 33 samples were obtained from these operators during their chamber exposures.

RESULTS

Chamber Characterization

CS concentrations ranged from 0.4 – 53.3 mg/m^3 ($\overline{x}$=10.4 mg/m^3) for 48 total samples, 12 from each location (Figure 4, A-D). The Shapiro-Wilk test indicated that the data were not normally distributed ($p<0.01$) and required non-parametric analysis (65). CS concentrations at sampling locations A-D were not statistically different when compared using the Kruskal-Wallis one way analysis of variance ($p=0.198$) (48). This is likely the result of mixing created by the constant movement of the trainees and chamber operators. These data suggest that CS is evenly dispersed across the four sampling points

and allows one area sample at a fixed location (Figure 4, A-D) to represent chamber concentrations. Location C was selected as the location nearest the center of the mask removal area.

Exposure Assessment

Table 1 shows the 134 area samples used as individual exposure surrogate measures for the 6,723 trainees in this study. Observed CS concentrations were not normally distributed ($p<0.01$) and ranged from 1.74 to 55.24 mg/m^3 ($\overline{x}$=9.9 mg/m^3) with exposure durations and sampling times ranging from 5.0 – 15.0 minutes ($\overline{x}$=8.7 min). Eight-hour time weighted averages (TWA) ranged from 0.02 to 1.21 mg/m^3 ($\overline{x}$=0.18 mg/m^3). All area samples (n=134) exceeded the ACGIH TLV-C [skin] (0.39 mg/m^3), 98% (n=131) exceeded the IDLH (2.0 mg/m^3), and 11% (n=15) exceeded the OSHA Permissible Exposure Limit (PEL) (0.4 mg/m^3). All trainees (n=6,723) in the cohort were potentially exposed to CS concentrations exceeding the ACGIH TLV-C [skin], 6,589 to concentrations exceeding the IDLH, and 770 to concentrations exceeding the OSHA PEL (Figure 6).

The results of the personal monitoring samples collected from the seven different chamber operators (A-G) are displayed in Table 2. One data point was excluded from the analysis because of a pump failure. Personal monitoring samples were not normally distributed ($p<0.01$) and ranged from 2.37 to 35.07 mg/m^3 ($\overline{x}$=10.3 mg/m^3) with exposure durations ranging from 28.0 – 90.0 minutes ($\overline{x}$=56.5 min). All samples exceeded the ACGIH TLV-C [skin] and the IDLH. The eight-hour TWAs for the chamber operators ranged from 0.3 to 5.0 mg/m^3 ($\overline{x}$=1.5 mg/m^3); 32 of 33 samples exceeded the OSHA PEL (Figure 6).

DISCUSSION

US Army doctrine dictates the exposure standards set forth by the OSHA will be adhered to unless the exposure standards set by the ACGIH are more protective; the ACGIH TLV-C, the OSHA PEL and the NIOSH IDLH are applicable to CS exposures (24). The TLV-C (0.39 mg/m^3) is a value that should not be exceeded during any part of the exposure scenario and was established to minimize CS-induced damage to the respiratory epithelium and protect against symptoms including burning of exposed skin and potential skin sensitization (3; 4). The OSHA PEL (0.4 mg/m^3) is the average concentration exposure during an eight-hour work period that should not be exceeded during a 40-hour work week and was developed to reduce the risk associated with skin, eye, and respiratory effects (2; 59; 61). The NIOSH IDLH (2.0 mg/m^3) was established to prevent delayed or permanent health effects (including death) associated with exposure and to protect against eye, respiratory, and other effects that could prevent escape from the exposure scenario (53).

The primary routes of trainee exposure are inhalation (respiratory tract) and absorption (skin and eyes) (57). Exposures to the respiratory tract and eyes may have occurred if a mask was defective or improperly sealed, when required to break the seal of the mask, or when required to remove the mask prior to exiting the chamber. Army safety guidelines state "Unprotected personnel will not be exposed to riot control agents longer than 15 seconds"; however, observed time out of mask for 34 randomly selected participants from different companies ranged from 29 – 122 seconds ($\overline{x}$=48.9 s) (29). Skin exposures occur continuously with hands, wrists, necks and backs of the head fully exposed to airborne CS. The ACGIH advises that when a chemical bears a skin notation,

measures should be taken to prevent dermal contact because air sampling does not account for exposure contributions via the cutaneous route (4). Furthermore, CS penetrates and remains in uniform fabric, presenting potential longer-term exposures. These factors suggest that trainees are potentially exposed to CS at levels greater than those indicated by the air monitoring results presented here.

It is common practice to monitor workers closest to the point of generation (chamber operators) with the assumption of a worst-case exposure scenario (58). Since the data presented here show chamber operators are overexposed, the potential for similar trainee overexposure is possible and consistent with the area sampling data presented in Table I. It is important to note however, that full-period sampling was used to monitor the chamber operators. This sampling methodology provides the mean concentration each chamber operator was exposed to during a particular chamber exercise. Changes in concentrations created by addition of CS, doors opening, trainees exiting and general mixing within the chamber are not individually captured, but averaged together. Consequently, chamber operators may have been exposed to higher CS concentrations than are reported here. Conversely, trainees had much shorter sampling durations which may have captured many of the aforementioned concentration changes. The difference in sampling durations resulted in a disparity in the observed concentration ranges for trainees versus chamber operators; however the Mann-Whitney U test failed to reveal a statistical difference between the mean trainee CS concentration ($\overline{x}$=9.9 mg/m^3) and the mean chamber operator CS concentration ($\overline{x}$=10.3 mg/m^3) at the 95% confidence level (p=.172).

Chamber operators are not required to break the seal or remove their mask; however, the question of respirator efficacy in this environment remains. The M40 is designed to protect the respiratory system from military chemical warfare agents. The Department of the Army and Department of Defense are the approval authority for respirators to be used for protection against these agents; however riot control agents are specifically exempt from this definition, leaving NIOSH as the approving authority (20). A quantitatively fit NIOSH approved full-face APR has an assigned protection factor (APF) of 50 and is capable to protect against airborne concentrations up to the IDLH; however, the M40 is not NIOSH approved and thus does not have an APF. Without an APF, it is difficult to determine whether the M40 provides adequate respiratory protection for concentrations approaching the IDLH level. When IDLH is exceeded, a full-face pressure demand self-contained breathing apparatus (SCBA) or a combination full- face pressure demand supplied air respirator (SAR) with auxiliary self-contained air supply is required (1; 14; 32; 57). Routine entry into this type of environment requires approval from either the installation medical authority or the safety and occupational health manager (20). Since chamber operators are exposed to levels exceeding the PEL and IDLH on a routine basis, they should be issued a NIOSH approved, quantitatively fit respirator and be enrolled in a respiratory protection program (1; 20; 25; 32; 59). All chamber operators in this study wore only a qualitatively fit-tested M40 series protective mask and were not enrolled in a respiratory protection program.

Chamber operators were also subjected to the effects associated with dermal exposure to CS. Three of the seven chamber operators wore the Mission Oriented Protective Posture (MOPP) level four ensemble without the chemical protective over

boots. MOPP level four features a chemical protective over garment that covers the upper and low body, chemical protective gloves and over boots, and the M40 series mask with attached hood (54; 72). The remaining four chamber operators (and three investigators) wore only the ACU and an M40 protective mask without a hood. Three of four chamber operators and two of three investigators who wore only the ACU and M40 protective mask without the hood developed erythema that persisted for up to 48 hours on the exposed skin on the back of the neck and head. These reactions are consistent with those from prolonged CS skin exposures (6; 12; 66).

CONCLUSION

This study is the first to quantify CS exposures in US Army BCT trainees and chamber operators. Both cohorts were potentially exposed to CS levels requiring a greater level of respiratory and skin protection than afforded at the time of this study. All members of the BCT cohort were potentially exposed to CS concentrations exceeding the TLV-C [skin], 98% of which exceeded IDLH. This is consistent with previous unoccupied chamber studies that suggested the US Army MCT procedures produce CS concentrations exceeding guidelines established by the ACGIH, NIOSH, and OSHA (40).

A work practice control of decreasing the concentration of CS used in the MCT may reduce the potential for overexposure to CS. Mask Confidence Training's primary goal of demonstrating the capability of the protective mask can be accomplished using CS concentrations bounded by the odor threshold (0.004 mg/m^3) and the TLV-C (0.39 mg/m^3) (23; 38). If concentrations remain within this range, the need for skin and respiratory protection are greatly decreased. Chamber CS concentrations should be evaluated by industrial hygiene personnel at least annually to verify exposure levels (25).

Pairing this with administrative controls such as rotating chamber operators and limiting the time trainees are inside the chamber without respiratory protection to 15 seconds should significantly reduce overexposure potential.

If CS concentrations are not reduced, personal protective equipment must be relied upon to reduce exposures. The use of the chemical protective garment ensemble by both the trainees and operators should reduce potential skin exposures. Respiratory exposures may be minimized through proper mask maintenance, quantitative fit testing, and equipping chamber operators with NIOSH certified masks designed to protect them against levels of CS exceeding IDLH. Chamber operators should also be enrolled in a respiratory protection program.

The results of this study prompted the March 2013 publication of All Army Activities (ALARACT) message 051/2013, which incorporated several of the controls recommended here into future Army MCT events. Specifically, it reduced the number of CS capsules required to charge the chamber, reduced the number of capsules used to maintain the CS concentration, and specified a maximum time out of mask of 15 seconds. It also mandated semi-annual industrial hygiene assessments of all Army mask confidence chambers and periodic wet cleaning of said chambers (75).

Ongoing research is being conducted to investigate health effects associated with the CS exposures documented here. Future research is needed to quantify CS exposure levels after implementation of ALARACT 051/2013 to determine if the controls were effective in lowering CS concentrations and to study the effect of these controls on health outcomes.

DISCLAIMER

The views expressed in this article are those of the authors and do not reflect the official policies or positions of the Uniformed Services University of the Health Sciences, Department of the Army, Department of Defense, or the US Government.

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Table 1. CS Concentrations and Exposure Durations for Trainees

Company #	Exposure Group 1 n	Time (min)	CS (mg/m^3)	Exposure Group 2 n	Time (min)	CS (mg/m^3)	Exposure Group 3 n	Time (min)	CS (mg/m^3)	Exposure Group 4 n	Time (min)	CS (mg/m^3)
1	55	10.1	13.0	53	8.5	17.2	56	10.0	12.7	54	10.0	5.3
2	47	10.0	7.3	47	8.7	7.7	46	8.0	8.3	45	8.0	7.4
3	55	9.0	53.3*	55	8.0	12.6	52	7.0	12.4	56	8.0	10.0
4	55	7.5	20.4	56	6.5	45.1*	54	8.0	43.3*	55	10.0	23.3*
5	53	9.0	5.0	55	7.5	5.3	48	7.0	5.3	54	8.5	5.0
6	50	9.0	25.9*	49	9.0	48.2*	50	10.0	29.3*	49	10.0	20.0*
7	45	5.5	14.9	48	7.0	13.1	50	10.0	24.0*	44	10.0	12.5
8	51	9.0	3.6	53	7.0	7.8	55	10.5	11.2	52	10.5	6.2
9	51	6.0	9.8	51	7.0	12.5	52	6.0	17.9	50	5.0	9.9
10	51	7.0	9.0	51	7.5	5.4	57	8.5	4.7	55	10.0	4.1
11	52	9.0	19.6	52	10.0	34.0*	51	10.5	55.2*	51	10.0	7.8
12	43	10.0	20.1*	45	10.0	25.0*	41	9.0	24.2*	44	10.0	16.6
13	53	8.5	4.2	51	7.5	4.5	56	8.0	5.3	56	10.0	5.3
14	60	7.5	3.3	55	8.0	2.6	52	7.0	3.2	63	10.5	2.6
15	57	7.5	5.7	59	6.5	8.4	60	10.5	8.1	58	10.0	6.4
16	67	10.5	6.2	68	9.0	6.0	67	8.5	5.7	No Exposure Group		
17	48	7.5	5.2	46	8.5	4.4	49	8.5	4.0	47	6.5	3.5
18	48	8.0	3.9	48	10.0	4.0	48	8.5	3.6	49	9.5	4.0
19	47	7.0	6.0	46	7.0	2.9	45	8.0	3.3	46	10.0	3.0
20	40	10.0	1.7	41	8.0	4.4	39	8.0	5.1	45	6.0	2.8
21	48	9.0	18.5	46	7.0	10.1	46	6.5	7.6	43	8.0	7.0
22	38	8.0	5.0	39	7.5	4.5	40	6.5	2.6	46	8.0	4.1
23	48	7.0	8.8	47	7.0	8.0	44	6.5	7.3	48	8.5	6.6
24	48	8.0	3.6	51	9.0	11.4	48	9.0	7.7	8	7.0	3.2
25	47	10.0	1.9	49	10.0	5.7	49	10.0	5.7	53	8.5	8.6
26	51	10.0	2.7	49	10.5	13.1	45	11.0	13.9	49	11.5	7.5
27	39	7.5	6.7	50	10.5	6.4	53	8.0	6.6	50	8.0	7.2
28	53	9.0	19.3	54	11.0	12.3	43	8.5	10.4	70	15.0	16.9*
29	45	7.0	4.1	44	7.5	3.8	57	8.5	4.9	58	8.5	5.6
30	43	6.5	2.6	47	6.0	1.8	50	6.0	4.7	64	7.5	5.5
31	54	8.5	6.9	49	9.0	5.5	46	9.0	4.0	51	11.0	5.6
32	59	13.0	3.6	61	13.0	5.6	65	13.0	7.7	No Exposure Group		
33	46	9.0	3.3	47	9.5	2.2	49	9.5	3.1	50	11.5	2.9
34	46	10.0	7.3	55	9.5	7.0	57	9.0	6.4	29	7.0	5.1

Exceeded ACGIH TLV-C (0.39 mg/m^3)

Exceeded NIOSH IDLH (2.0 mg/m^3)

*Exceeded OSHA PEL (0.4 mg/m^3) when averaged over the eight-hour work day

Table 2. CS Concentrations, Exposure Durations, and TWAs for Chamber Operators

Company #	Chamber Operator ID	Time (min)	CS (mg/m^3)	TWA (8 hr)	Company #	Chamber Operator ID	Time (min)	CS (mg/m^3)	TWA (8 hr)
1	B	70.0	11.1	1.6	18*	D	57.0	2.8	0.6
2	C	48.0	6.8	0.7	19	D	46.0	10.0	1.0
3	A	54.0	7.7	0.9	20	E	51.0	3.6	0.4
4	A	54.0	32.2	3.6	21	G		Pump Failure	
5	C	53.0	6.5	0.7	22*	D	49.0	2.4	1.1
6	A	69.0	35.1	5.0	23*	D	41.0	10.1	1.1
7	A	28.0	15.0	0.9	24	E	50.0	9.9	1.0
8	A	83.0	9.1	1.6	25*	F	64.0	12.7	2.6
9	A	83.0	15.7	2.7	26*	F	71.0	6.1	2.6
10	A	54.0	10.3	1.2	27	D	50.0	10.5	1.1
11	B	90.0	21.4	4.0	28	F	62.0	15.1	2.0
12	A	87.0	19.5	3.5	29	D	50.0	3.3	0.3
13*	E	52.0	7.3	1.2	30	D	41.0	6.0	0.5
14*	E	56.0	3.1	1.2	31	G	46.0	5.4	0.5
15	E	60.0	9.7	1.2	32	F	47.0	6.1	0.6
16	D	46.0	11.5	1.1	33	G	55.0	5.0	0.6
17*	D	50.0	2.9	0.6	34	D	48.0	6.7	0.7

Exceeded OSHA PEL (0.4 mg/m^3)

Exceeded ACGIH TLV-C (0.39 mg/m^3) and NIOSH IDLH (2.0 mg/m^3)

*Companies 13&14, 17&18, 22&23, and 25&26 occurred in the same eight-hour workday respectively

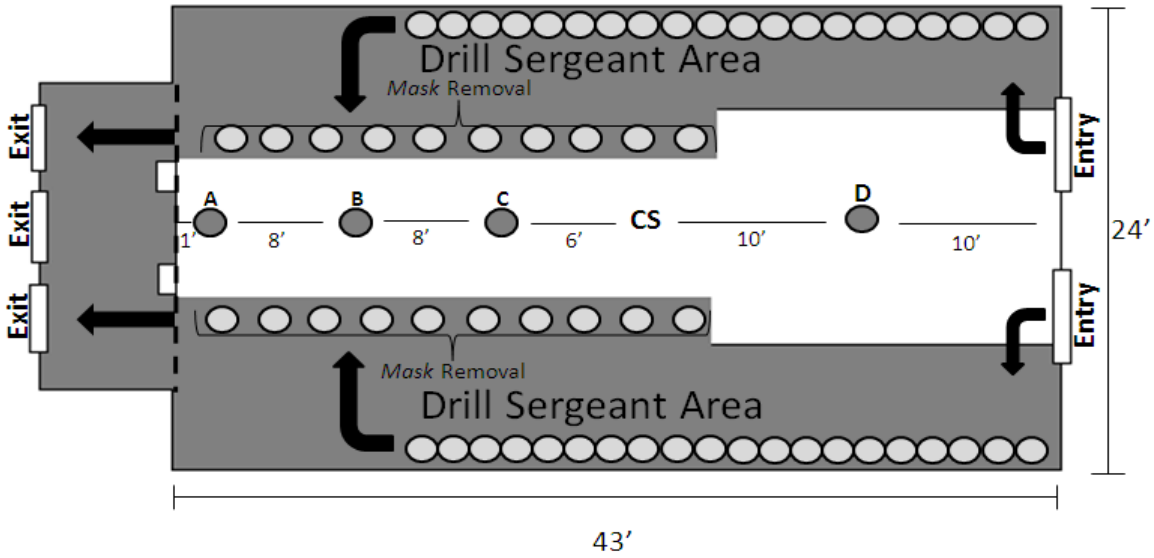

Figure 4. Fort Jackson Mask Confidence Chamber.
Dark circles A-D represent sampling locations; light circles represent trainees; white represents the area open to sampling; and arrows depict the flow of trainees through the chamber.

Figure 5. Hot plate method of CS dispersion at the Fort Jackson mask confidence chamber.

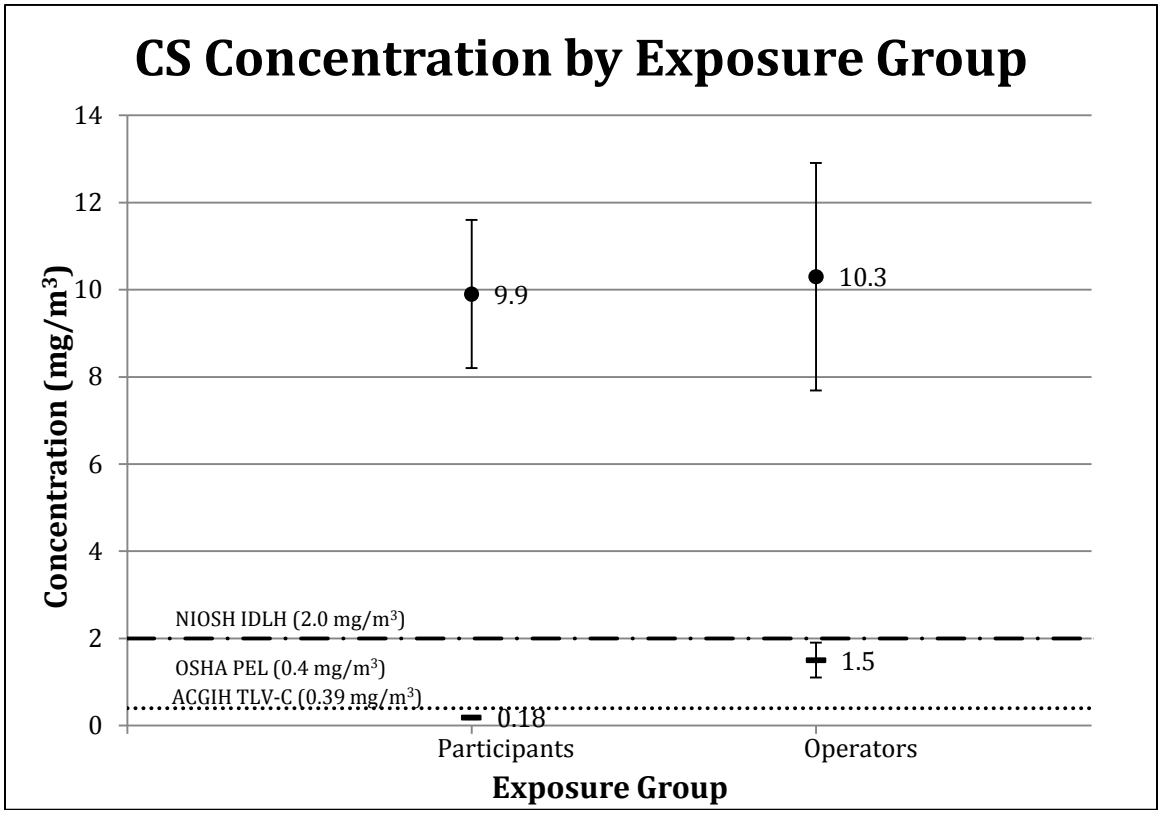

Figure 6. CS Concentration by Exposure Group.

● represents mean exposure concentration, ▬ represents mean eight-hour TWA; error bars represent 95% confidence interval

CHAPTER 5: O-Chlorobenzylidene Malononitrile (CS Riot Control Agent) Associated Acute Respiratory Illnesses in a US Army Basic Combat Training Cohort

ABSTRACT

Acute respiratory illnesses (ARI) are among the leading causes for hospital visits and lost work time in United States (US) military training populations. ARI related hospital visits historically peak during weeks four through six of US Army Basic Combat Training (BCT) following mandatory exposure to the riot control agent o-chlorobenzylidene malononitrile (CS). This observational prospective cohort studied the association between CS exposures and ARI related health outcomes in 6,723 US Army recruits attending BCT at Fort Jackson, South Carolina from August 1 to September 25, 2012. Recruits had a significantly higher risk (RR=2.44, 95% CI=1.74, 3.43) of being diagnosed with ARI following exposure to CS compared to the period of training preceding exposure, and incidence of ARI after CS exposure was dependent upon the CS exposure concentration (p=0.03). There was a significant pre/post exposure ARI difference across all CS concentration levels (p=0.006), however no significant differences were detected among these rate ratios (p=0.72). Since CS exposure is positively associated with ARI health outcomes in this population, interventions designed to reduce or eliminate respiratory exposures could result in decreased hospital burden, health care costs, and lost training time in the US Army BCT population.

INTRODUCTION

Acute respiratory illnesses (ARIs), including the common cold, influenza, pharyngitis, laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia, and other

respiratory ailments, are a global medical concern. Lower respiratory tract infections alone account for over 429 million incident cases per year globally (second only to diarrheal diseases) and lead the world in disease burden (81). ARIs are a primary contributor to health loss in the United States (US) and are a significant source of morbidity in US military training populations (34; 50). ARIs accounted for more hospital visits and lost work time than any other illness or injury in US military recruits from 2010 to 2011 and were second only to injury and poisoning the following year (7; 8; 11).

The occurrence of ARIs in military recruit populations has been well studied; however, understanding of causal factors is limited (13; 33; 47; 71). A 1998 study of Army Basic Combat Training (BCT) at Fort Jackson, South Carolina found that nearly 50% of recruits sought medical care for ARI related conditions and over 90% of participants self-reported ARI symptoms. Respiratory related hospitalizations peaked during training weeks four and five, while self-reported febrile illnesses peaked during the third week of training. Investigators attributed the rise in ARI rates to a lapse in availability of an effective adenovirus vaccine (47). Another study, conducted in 2004, investigated the effect of building design on ARI rates in the BCT population at Fort Jackson, SC. Investigators determined that recruits living in 60-person rooms had a significantly greater ARI risk than those living in 8-person rooms, and that both febrile and afebrile ARI rates peaked during weeks four through six of the training cycle. Investigators concluded the week of training was significant at almost all levels, across genders, and for both febrile and afebrile ARI outcomes. The authors hypothesized the observed increase in ARI incidence was due to previously unencountered respiratory pathogen exposure, crowded living and training conditions, and decreased immune

function due to physical and emotional stress related to entering military training. Immunity increased as the training cycle progressed and trainees adapted to their new environment. This study acknowledged the potential role of training in ARI trends, but did not identify specific training events that may have impacted the reported ARI rates (80).

In the early 1990s, British Surgeon Lieutenant Commander Pipkin described an ARI outbreak in a Royal Marines training population where cases of influenza peaked shortly following exposure to the riot control agent o-chlorobenzylidene malononitrile (CS) (62). CS has a profound effect on the respiratory system, causing immediate pain and irritation in the nose and mouth, excessive nasal discharge and salivation, and sometimes violent coughing spasms, damage to the respiratory epithelium, and pulmonary edema (67; 69). Pipkin speculated that a combination of these effects may have increased influenza incidence within the exposed Royal Marines (62). The biological plausibility of this hypothesis is reasonable, as opportunistic respiratory infections (including those associated with ARI) have been shown to spread via direct and indirect contact, and to commonly occur following chemical irritation or injury (5; 80). Unfortunately, due to a small sample size, Pipkin's hypothesis could not properly be tested, and the question of whether CS exposure can increase ARI rates remains unanswered.

Currently, no ARI studies have considered exposure to CS as a covariate in analyses. All US Army BCT soldiers are exposed to CS in the first three weeks of BCT. A 2012 study of over 6,500 Soldiers participating in mask confidence training during BCT at Fort Jackson, SC showed that unmasked recruits were exposed to CS

concentrations over 125 times the American Conference of Industrial Hygienist (ACGIH) Threshold Limit Value Ceiling (TLV-C) and over 25 times the National Institute for Occupational Safety and Health (NIOSH) Immediately Dangerous to Life and Health (IDLH) level (41). These limits were established to protect against irreversible health effects and prevent damage to the respiratory epithelium (40). High levels of acute CS exposure in Army BCT prior to the observed increase in ARI rates, make it temporally plausible that CS exposure experienced during mask confidence training could induce chemical damage to the respiratory tract that is diagnosed as ARI or increase susceptibility to ARIs, both of which would result in an increase in ARI incidence. It is also possible that CS-induced expectoration promotes the spread of pathogens responsible for ARI in this population.

This study examines the association between CS exposure concentrations and ARI health outcomes during Army BCT. The study protocol was approved by the United States Army Training and Doctrine Command (TRADOC) and the Uniformed Services University of the Health Sciences (USU) and was deemed non-human subject research by the USU Institutional Review Board (IRB) due to the observational nature of the study and lack of personal identifying information available to the investigators. This work was sponsored by the US Army Medical Command, Office of the Surgeon General (MEDCOM/OTSG), Falls Church Virginia. No additional funding was received.

METHODS

This study used an observational, prospective cohort design in a gender integrated cohort of 6,723 exposed recruits attending US Army BCT at Fort Jackson, SC from August 1 to September 25, 2012 to capture the incidence and distribution of ARI before

and after completion of the mandatory mask confidence training (MCT) portion of their initial military training.

Army training units, designated as approximately 200-person “Companies”, scheduled for MCT were identified by Unit Identification Code (UIC) through coordination with staff at the Chemical, Biological, Radiological, and Nuclear (CBRN) training range. Data on the type of barracks and training week were captured from administrative records provided by Fort Jackson training officials.

Upon arrival to the training site, training units were divided into four ad hoc exposure groups consisting of approximately 50 personnel to proceed through the mask confidence chamber. Exposure group assignment, composition, and size were determined by training officials and were not influenced by investigators. CBRN staff aerosolized 10 CS capsules to establish an initial concentration of CS inside the chamber; the first exposure group entered, conducted a series of exercises, removed their protective masks, and exited the chamber. CBRN staff then aerosolized one additional CS capsule for every 10 people that exited the chamber and the next exposure group entered (41). This process continued until all four exposure groups completed the training event.

Officials from each training unit used a personnel roster to document trainee attendance, exposure group (1-4), and completion of the chamber exercise. Trainees who completed MCT with their assigned training unit were enrolled in the cohort; absent soldiers or those who completed the training but were from a different training unit were excluded. Count data specifying the number of trainees that completed the chamber exercise and the number of trainees in each exposure group was provided to the investigators after each training event. CS concentrations were obtained for each

exposure group from a concurrent industrial hygiene study (41). Exposure groups were categorized as one of four exposure categories: 0.00-2.00 mg/m^3, 2.01-5.00 mg/m^3, 5.01-10.00 mg/m^3, and greater than 10.00 mg/m^3 based on the IDLH value (2.00 mg/m^3) and the incapacitating range (5.00 – 10.00 mg/m^3) outlined in US Army manuals (23; 53).

Clinically diagnosed and documented inpatient and outpatient ARI (both febrile and afebrile) were the outcomes of interest. Medical staff queried the Composite Healthcare Computer System (CHCS) for ARI encounters within companies that completed MCT using the following International Classification of Diseases Version 9 (ICD-9) codes: 079.99 Viral infection, not otherwise specified (NOS); 382.9 Otitis media NOS; 460 Nasopharyngitis, acute; 461.9 Acute sinusitis; 465.8 Acute upper respiratory infections of other multiple sites; 465.9 Acute upper respiratory infections of unspecified site; 466.0 Bronchitis, acute; 486 Pneumonia, organism NOS; 487.0 Influenza with pneumonia; 487.1 Influenza with respiratory manifestation, not elsewhere classified (NEC); 487.8 Influenza with manifestation NEC; 490 Bronchitis NOS; 784.1 Pain, Throat; and 786.2 Cough.

Surveillance count data by training unit was provided by local preventive medicine personnel as part of the existing Acute Respiratory Disease (ARD) surveillance program (27). No personal identifying information was provided to the investigators. The surveillance period began seven days prior to CS exposure and ended seven days after exposure (including the day of the exposure). Occurrence of one or more of the ARI related ICD-9 codes as the primary or secondary diagnosis in a trainee's electronic medical record during the surveillance period was designated as case. This case definition captured both febrile and afebrile ARI cases. Febrile ARI cases had oral

temperature of 100.5° F or higher and at least one sign or symptom of acute respiratory tract inflammation (i.e. sore throat, cough, runny nose, chest pain, shortness of breath, headache, tonsillar exudates or tender cervical lymphadenopathy) (27). All cases not meeting this definition were categorized as afebrile. Cases were further divided into pre and post-chamber ARI cases. A pre-chamber ARI case was defined as occurring within a training unit in the seven day period prior to CS exposure. A post-chamber ARI case was a case that occurred during the seven day surveillance period beginning with exposure to CS in the mask confidence chamber.

To prevent counting multiple encounters by an individual and ensure the most severe health outcomes were captured, first diagnosis of ARI during the surveillance period was used to establish pre or post-chamber ARI status. However, if a later febrile ARI diagnosis occurred, it took priority and was used to establish pre or post-chamber ARI case status. Those designated as pre-chamber cases were treated as non-susceptible for post-chamber ARI risk calculations. Cases were cross-referenced with training rosters to determine their cohort and exposure group status. Local preventive medicine personnel provided case counts by training unit, febrile/afebrile, exposure group, and date of encounter.

These counts, along with previously gathered information, were entered into SPSS Statistics for Windows (Version 19, IBM Corp., 2010) for data management. Chi-squared analyses, stratified risks, risk ratios (RR) and their 95% confidence intervals (95%CI) were calculated using Open Source Epidemiologic Statistics for Public Health (Version 3.01, www.openepi.com., 2013). SPSS was used to conduct a Poisson Regression analysis to examine the relationship between CS exposure concentration and

the outcome of interest since ARI count data and time to ARI diagnoses following CS exposure were variables in the analysis. Power calculations determined a minimum of 64 exposure groups were required to detect a 0.5 difference in risk at 80 percent power.

RESULTS

There were a total of 6,723 recruits divided into 134 exposure groups during the surveillance period. All members of the cohort were exposed to CS in the first three weeks of training and lived in one of three building types: 1) Starship barracks (SS) – Fixed facilities consisting of 60 person rooms; 2) Relocatable barracks (RL) – Movable facilities that can accommodate up to 50 recruits per room; or 3) Rolling Pin barracks (RP**) –** Fixed facilities consisting of eight-person rooms**.** Over half (55.9%) of the cohort completed the mask confidence chamber during their second week of training and most (58.0%) lived in the SS style barracks. Only one training unit consisting of 165 recruits was housed in the RP style barracks. There were a total of 161 clinically diagnosed cases of ARI in the study population; 47 occurred prior to CS exposure and 114 after (Table 3). Only four (2.48%) of these cases were coded in CHCS as febrile ARI cases; all of which occurred post-chamber. Figure 7 shows the distribution of post-chamber ARI cases by day.

Table 4 shows the overall risk of developing ARI after exposure to CS was significantly higher than the risk of developing ARI in the surveillance period before completion of the mask confidence chamber (RR= 2.44, 95%CI=1.74, 3.43). Increased ARI risk was observed regardless of training week the mask confidence chamber was conducted or building the recruit lived in. The Breslow-Day test for interaction of risk ratios over strata did not suggest interaction; stratum specific Mantel Haenszel adjusted

rate ratios were not significantly different than the overall rate ratio suggesting a lack of confounding by chamber week or building type. Overall ARI, pre-chamber ARI, and post-chamber ARI incidence rates were not observed to be different across chamber weeks (p=0.92, p=0.98, p=0.85) and building types (p=0.17, p=0.72, p=0.17) (Table 4). A chi-squared analysis suggested post-exposure ARI cases are dependent upon CS exposure concentrations (p=0.03) (Table 5). A Poisson regression analysis showed a significant pre/post-chamber ARI difference across all concentrations higher than the referent level (0.00-2.00 mg/m^3) (p=0.006); however, no significant differences were detected among these rate ratios (p=0.72) (Figure 8).

DISCUSSION

The results of this study suggest that within our study population, exposure to CS resulted in nearly 2.5 times greater ARI diagnosis risk after MCT compared to the period of training preceding this event. Elevated ARI risk was independent of both the week of training in which CS exposure occurred and barracks building type.

Over 95 percent of the cohort was exposed to CS in excess of IDLH (2.00 mg/m^3), with the majority of the population (70.0%) exposed at levels greater than 2.5 times IDLH (41). The risk of being diagnosed with a post-chamber ARI compared to being diagnosed pre-chamber was significantly elevated in all exposure concentration levels exceeding IDLH. These risks were not statistically different from each other, thus a dose response relationship could not be established (p=0.72); however, post-chamber ARI incidence was dependent upon CS exposure concentrations (p=0.03).

The incidence of both pre-chamber ARI (2.24%, 95%CI=0.47, 6.81) and post-chamber ARI (2.29%, 95%CI=0.48, 6.81) were elevated in exposure concentrations

below IDLH when compared to other groups. However, it is important to note the lack of statistical significance may be due to the sparseness of data at this lowest exposure group (n=134). Also, ARI present in the pre-chamber (unexposed) population cannot be temporally linked to CS exposure. One possible link could be mixing of the population with CS exposed cases returning to a military unit before it attends the mask confidence chamber, but this was not observed during the conduct of this study.

The increased risk observed at concentrations above IDLH suggests that there may be a threshold concentration in the range of 0.00 – 2.00 mg/m^3 that prompts symptoms that could result in an ARI diagnosis. It may also suggest that the IDLH value (2.00 mg/m^3) set by NIOSH is protective against ARI. A decreased risk (RR=1.02, 95%CI=0.21, 4.98) was observed at concentrations below IDLH; however, since only 134 (1.99 %) of the entire cohort was exposed at levels below IDLH, it is difficult to determine whether this decreased risk was observed by chance alone. Future studies are needed to better characterize the ARI risk associated with this CS concentration range.

Week of training and living environment have been associated with increased risk of both febrile and afebrile ARI outcomes in a BCT population (47; 80). The results of this study however, suggest that these covariates do not play a significant role in ARI outcomes during the first three weeks of BCT. Pre-chamber, post-chamber, and overall ARI incidence rates did not vary by week or building type and the pre/post-chamber ARI rate ratio was the same across these strata.

One potential explanation for the lack of significance of these covariates is seasonality. Previous studies were conducted in close proximity to the cold and flu season (47; 80). These populations may have been exposed to a greater number of

infectious ARI causing pathogens whose transmission (via direct and/or indirect mechanisms) could be influenced by living and sleeping arrangements. Furthermore, in this scenario, it would take time for infectious ARI to build within a training unit, thus making week of training a relevant factor. This study was well removed from the cold and flu season and experienced an ARI cumulative incidence of only 2.40% (0.06% febrile, 2.34% afebrile) over the study period.

A more likely reason for the disparity in relevant covariates in this study when compared to previous work is the implementation of a new vaccine in November, 2011 that targeted Adenovirus types 4 and 7 and significantly decreased ARI incidence in the BCT populations across all military services (8; 10; 35). The impact of the vaccine was evident in this study with only four febrile ARI cases and both febrile and afebrile incidence rates considerably lower than the historic incidence rates (47; 80). The majority of febrile cases (3 of 4) resided in the SS style barracks, which was consistent with previous research (80). All four cases occurred after completion of the mask confidence chamber at exposure concentrations greater than 2.5 times the IDLH, suggesting that exposure to elevated CS concentrations may increase febrile ARI risk. The low febrile case count, however, could suggest that CS induced respiratory tract injury rather than infection may have contributed to the number of post-chamber ARI diagnoses in this population. However, since symptoms associated with CS exposure are generally short-lived and resolve themselves as time from exposure increases, one would expect CS injury induced ARI diagnoses to occur immediately following exposure. Our data show that only three (2.63%) post-chamber ARI cases were diagnosed the day of the chamber and only 19 (16.67%) were diagnosed the following day. This may suggest that

infection rather than CS induced injury was more prevalent in post-chamber ARI diagnoses.

There are several limitations associated with this study. To begin with, it was strictly observational and did not allow for the collection of personal characteristics (e.g. body mass index, prior smoking status, sex, etc.) that have been shown to influence ARI outcomes. Another potential confounder was re-use of protective masks by trainees during mask confidence training. Mid-way through the study period, investigators witnessed recruits exit the chamber and transfer their protective mask to waiting recruits whose originally issued masks were defective. Most masks were exchanged after quickly wiping with one antibacterial wipe; however some masks were not wiped at all. This practice introduced a potential avenue for the spread of ARI causing pathogens and was not controlled for in the study. Another limitation is that it relied on ARI incident estimates based upon ICD-9 codes in the recruit's electronic medical records, and did not include laboratory-confirmed ARI diagnosis. Without laboratory-confirmed pathogen specific diagnosis, CS induced injury of the respiratory tract could have easily been misdiagnosed as infection. In addition, the follow-up period may not have been long enough to identify these misdiagnosed cases or other afebrile ARI that may have progressed to febrile ARI later in the training cycle. A combination of these factors makes it extremely difficult to determine whether the cases captured in this study are a result of infection or injury. Finally, exposure concentrations were assigned based upon an area sampling methodology which assumed that CS was evenly dispersed in the mask confidence chamber (41). Although this is considered an acceptable method for

estimating exposures, it is not as precise as individual monitoring and could have impacted the results observed here.

CONCLUSION

This is the first study to consider CS exposure as potential risk factor for ARI diagnoses in a BCT population. Regardless of the cause for diagnosis (injury or infection), ARIs have a significant impact on the health care system and on the readiness of today's fighting force. This study showed that those exposed to CS in the mask confidence chamber had nearly 2.5 times greater risk of being diagnosed with ARI after completion of this training event. It also suggests that post-exposure ARIs are dependent upon CS exposure concentration. Since ARI is positively associated with CS exposure in this population, interventions designed to reduce or eliminate the exposure could result in decreased hospital burden, health care costs, and lost training time within the BCT population. It is also possible that this study could have broader implications to other military populations and law enforcement personnel.

Preliminary results of this study were provided to medical and training officials at TRADOC, through the Army Public Health Command (APHC), resulting in an Army-wide intervention by the US Army Safety Office targeting CS exposure levels to mitigate the risks reported here. This intervention, All Army Activities (ALARACT) message 051/2013, was implemented in March 2013 mandating lower CS concentrations, shorter exposure times, semi-annual industrial hygiene surveys, and periodic wet cleaning of all Army mask confidence chambers.(75) Ongoing research is being conducted at the Uniformed Services University of the Health Sciences to determine the efficacy of this intervention in lowering CS exposure concentrations and mitigating the risks reported

here. Future research is required to determine how this intervention may impact a recruit's perception of the protective nature of their assigned CBRN protective equipment and to determine if this intervention reduced lost training time, healthcare costs, and hospital burden.

DISCLAIMER

The views expressed in this article are those of the authors and do not reflect the official policies or positions of the Uniformed Services University of the Health Sciences, Department of the Army, Department of Defense, or the US Government.

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Table 3. ARI Incident Cases by Chamber Week and Building Type.

	N (%)		
Overall	Pre-Chamber ARI	Post-Chamber ARI	Total Population
	47 (0.70)	114 (1.70)	6723 (100)
Chamber Week			
1	7 (0.66)	20 (1.89)	1065 (100)
2	26 (0.70)	60 (1.62)	3693 (100)
3	14 (0.71)	34 (1.73)	1965 (100)
Building Type			
SS	30 (0.77)	72 (1.86)	3900 (100)
RL	16 (0.60)	42 (1.58)	2658 (100)
RP	1 (0.61)	0 (0.00)	165 (100)

Table 4. ARI Rates (Per 100 person-weeks) by Chamber Week and Building Type.

	ARI Rates (95% CI)			
Overall	Pre-Chamber ARI	Post-Chamber ARI	ARI Incidence	Pre/Post Rate Ratio
	0.70 (0.52, 0.93)	1.71 (1.42, 2.05)	1.20 (1.03, 1.40)	2.44 (1.74, 3.43)
Chamber Week				
1	0.66 (0.29, 1.38)	1.89 (1.21, 2.92)	1.27 (0.86, 1.85)	2.88 (1.22, 6.77)
2	0.70 (0.48, 1.03)	1.64 (1.27, 2.10)	1.17 (0.95, 1.44)	2.32 (1.47, 3.67)
3	0.71 (0.41, 1.20)	1.74 (1.24, 2.43)	1.23 (0.92, 1.63)	2.45 (1.32, 4.54)
Mantel Haenszel Risk Ratio				2.44 (1.74, 3.43)
Breslow-Day Test for Interaction				p=0.91
Building Type				
SS	0.77 (0.54, 1.10)	1.86 (1.48, 2.34)	1.31 (1.08, 1.59)	2.42 (1.58, 3.69)
RL	0.60 (0.36, 0.98)	1.59 (1.17, 2.15)	1.09 (0.85, 1.41)	2.64 (1.49, 4.69)
RP	0.61 (0.00, 3.70)	0	0.30 (0.00, 1.88)	0
Mantel Haenszel Risk Ratio				2.44 (1.74, 3.43)
Breslow-Day Test for Interaction				p=0.61

Table 5. Chi-Squared Test for Independence of Pre and Post-Chamber ARI Cases by CS Concentration.

	Pre-Chamber ARI				**Post-Chamber ARI**			
Variable	Non-Case	Case	X^2	p value	Non-Case	Case	X^2	p value
CS Concentration (mg/m^3)			6.60	0.09			8.87	0.03
0-2	131	3			128	3		
2-5	1852	9			1832	20		
5-10	2773	23			2712	61		
>10	1920	12			1890	30		

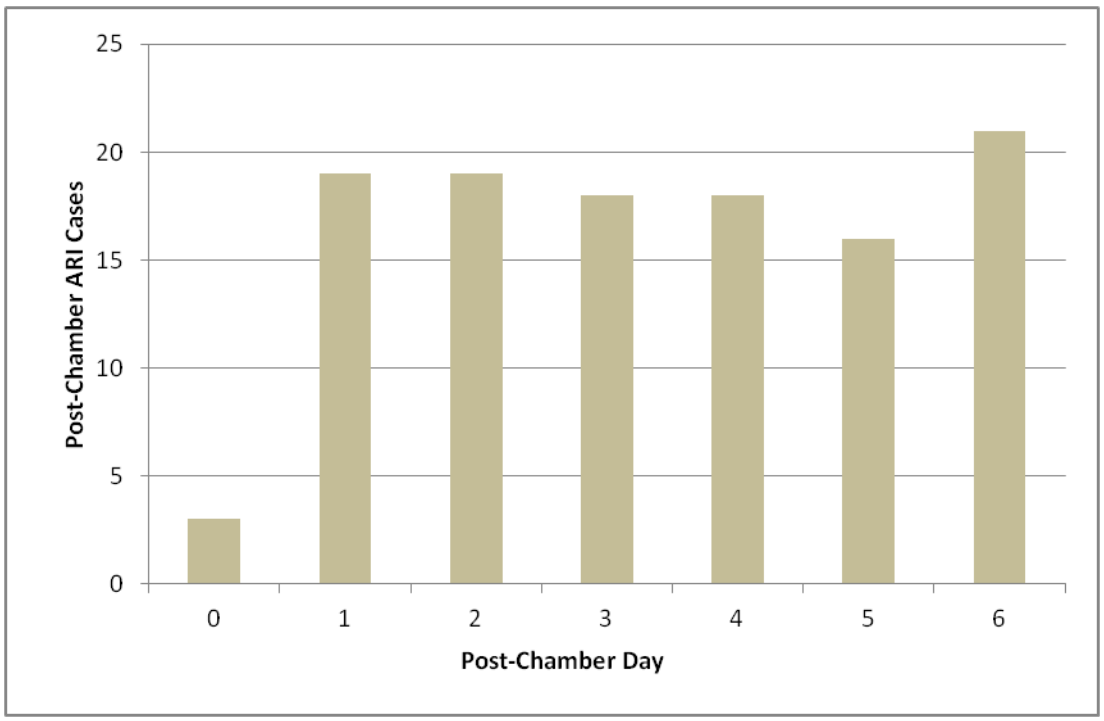

Figure 7. Distribution of Post-Chamber ARI by Post-Chamber Surveillance Day.

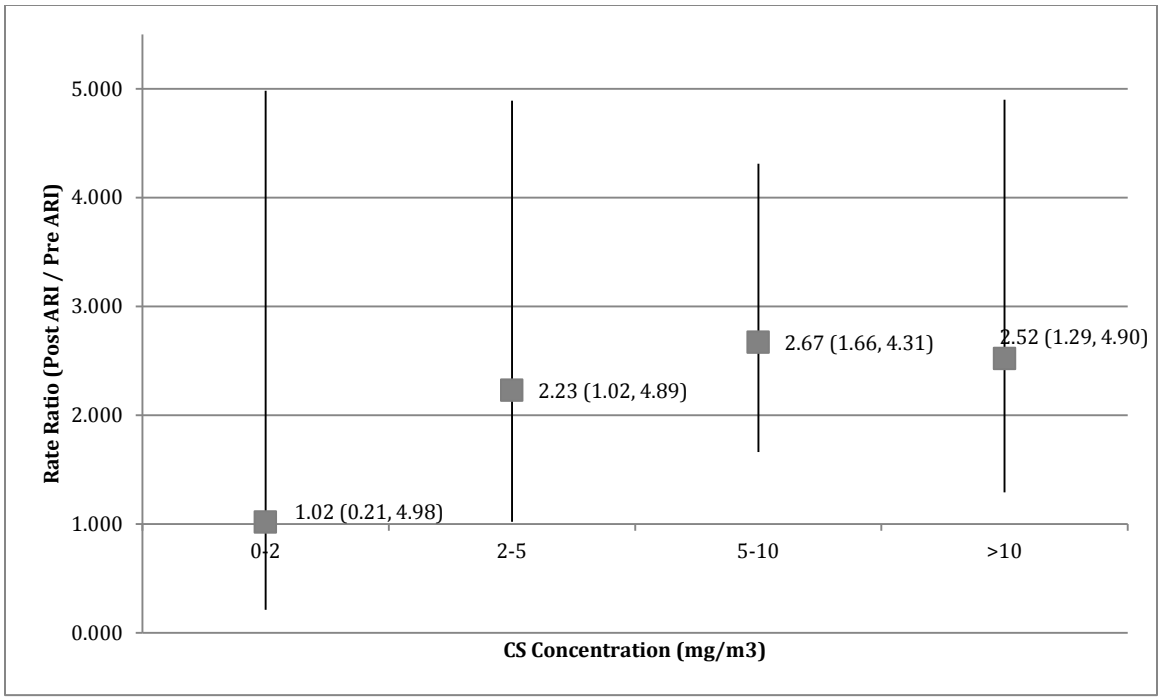

Figure 8. Relative Incidence of Post-Chamber ARI by CS Concentration and 95% Confidence Intervals.

CHAPTER 6: Evaluation of an Intervention Designed to Reduce O-Chlorobenzylidene Malononitrile (CS Riot Control Agent) Exposures and Associated Acute Respiratory Illnesses in a US Army Basic Combat Training Cohort

ABSTRACT

Exposing unmasked US Army recruits to o-chlorobenzylidene malononitrile (CS tear gas) during Mask Confidence Training (MCT) at concentrations exceeding the Immediately Dangerous to Life and Health (IDLH) level established by the National Institute for Occupational Safety and Health (NIOSH) increases the risk of Acute Respiratory Illness (ARI) diagnosis in the period following CS exposure when compared to the period before exposure. All Army Activities Message (ALARACT) 051/2013 was implemented in March 2013 to reduce CS exposure concentrations during MCT and associated ARI rates. This observational, prospective cohort studied CS exposures and associated ARI health outcomes after implementation of ALARACT 051/2013 in 5,298 US Army recruits attending Basic Combat Training (BCT) at Fort Jackson, SC from 13 March to 30 April, 2013. These data indicate a 10-fold reduction ($p<0.001$) in CS exposure concentrations following this intervention. Recruit exposures ranged from 0.26 – 2.78 mg/m^3 ($\overline{x}$=1.04 mg/m^3) and chamber operator exposures from 0.05 – 2.22 mg/m^3 ($\overline{x}$=1.05 mg/m^3). The overall risk of being diagnosed with ARI following CS exposure also decreased, but was still significantly higher in the seven days following exposure to CS when compared to the seven-day period before the exposure (RR=1.79, 95%CI=1.29, 2.47) resulting in 26.85% (95%CI=-0.17, 0.54) intervention effectiveness. Post-chamber ARI rates ($p=0.02$) were dependent upon CS exposure concentration, and pre/post-chamber ARI rate ratios were significantly elevated at all concentration categories higher than the Threshold Limit Value Ceiling (TLV-C) (0.39 mg/m^3). Results support findings

from previous research suggesting risk of ARI diagnosis after CS exposure is positively associated with CS concentration.

INTRODUCTION

All recruits entering the United States (US) Army are exposed to the riot control agent o-chlorobenzylidene malononitrile (CS) during mandatory Mask Confidence Training (MCT) in Basic Combat Training (BCT) and throughout their careers during annual Chemical, Biological, Radiological and Nuclear (CBRN) refresher training (38; 40). MCT takes place in a relatively air-tight structure commonly referred to as the gas chamber, where a CS-rich environment is created and maintained by thermally dispersing CS on an improvised aerosol generator. Soldiers wearing military respirators equipped with filters designed to protect against airborne chemical warfare agents enter the chamber, perform exercises specified by instructors inside the chamber, and finally remove their protective masks before exiting the chamber (22; 26). Soldiers feel almost immediate effects of CS upon mask removal (burning of the respiratory system, lacrimation, coughing, and sometimes vomiting) which demonstrates how a properly fitted protective mask shields the user from airborne chemical hazards (23; 30).

A recent study of 6,723 recruits attending Army BCT at Fort Jackson, SC showed the standard Army method used to conduct the MCT resulted in exposure of 100% of the study population to CS concentrations exceeding the American Conference of Industrial Hygienists (ACGIH) Threshold Limit Value-Ceiling (TLV-C) (0.39 mg/m^3). In addition, 98% of the study population also exceeded the limit (2.0 mg/m^3) deemed Immediately Dangerous to Life and Health (IDLH) by the National Institute for Occupational Safety and Health (NIOSH)(4; 41; 53). Researchers discovered recruits were exposed on

average to CS concentrations approximately five times higher than IDLH. Measured exposure levels ranged from 1.74 – 55.24 mg/m^3 and recruits were exposed for periods as long as two minutes without respiratory protection. Investigators recommended several industrial hygiene controls to protect recruits including lowering CS concentrations, increasing personal protective equipment, and reducing unprotected recruit exposure time to 15 seconds (41).

In a concurrent research effort, recruits from the aforementioned study were observed to determine whether elevated CS exposure concentrations were associated with increased incidence of Acute Respiratory Illnesses (ARI) in Army BCT. Researchers found 2.44 times higher risk of recruits being diagnosed with ARI in the seven day period following exposure to CS when compared to the seven days preceding exposure. The observed increased ARI risk was independent of week of training or the type of building they lived in. Post-exposure ARI incidence was dependent on CS exposure concentration and pre/post-exposure risk ratios appeared to increase with concentration to a threshold; however a statistically significant dose-response relationship could not be established. Researchers concluded that lowering CS exposure concentration in the MCT could lower ARI rates and decrease lost training time and health care costs within this BCT population (39).

Preliminary results of both of these studies were presented to US Army medical and training officials through the Army Public Health Command (APHC), resulting in the publication of All Army Activities (ALARACT) message 051/2013. ALARACT 051/2013 was implemented across the US Army in March 2013 to serve as an intervention to address the elevated CS concentrations and ARI risks found at Fort

Jackson. The ALARACT incorporated several recommendations made by researchers including reduction of CS used during MCT and maximum 15 second unprotected exposure times. In addition, it mandated semi-annual industrial hygiene surveys and periodic wet cleaning of MCT chambers across the Army(75). The present study was conducted after implementation of ALARACT 051/2013 and was designed to evaluate the efficacy the intervention to lower CS exposure concentrations and MCT associated ARI risk.

METHODS

This observational, prospective cohort study quantified CS exposure concentrations as well as incidence and distribution of ARI before and after CS exposure to explore the association between CS exposure concentrations and ARI health outcomes in a gender integrated cohort of 5,298 recruits completing mandatory MCT during US Army BCT at Fort Jackson, S.C. from 13 March to 30 April 2013. It further compared both CS exposure concentrations and ARI incidence results with those observed before implementation of ALARACT 051/2013 to evaluate intervention effectiveness. The study protocol was approved by the US Army Training and Doctrine Command (TRADOC) and the Uniformed Services University (USU) Office of Research, and was considered non-human subject research by the USU Institutional Review Board (IRB)(55).

Mask confidence training was scheduled by BCT companies (groups of approximately 200 recruits) through coordination with Chemical, Biological, Radiological and Nuclear (CBRN) staff operating the Fort Jackson MCT. Typically, training was scheduled during the first three weeks of BCT at the rate of one company per day. Fort Jackson training officials provided investigators with company MCT dates,

BCT start dates, and barracks types by unit identification code (UIC) prior to each scheduled MCT event.

On the day of the mask training, CBRN staff divided training units into four exposure groups of about 50 recruits each due to the limited size of the mask confidence chamber (described by Hout *et al.*); investigators did not influence exposure group size or composition(39). Groups were then staged outside of the mask confidence chamber where they donned their protective masks and were inspected for functionality by CBRN staff prior to entering the chamber (41).

CBRN staff pre-heated an inverted metal container to a mean temperature of 199^{o} C on an electric hot plate (General Electric model# 169214) positioned on a 1.10 m metal table in the center of the chamber. After approximately five minutes, the contents of three 650 mg CS capsules were poured directly into the can causing immediate CS dispersion. CS was not agitated with a stirring rod as observed in previous studies and visibly aerosolized in less than three minutes. The first exposure group then entered the mask confidence chamber, lined up against the walls, performed various exercises specified by training staff, and finally removed their protective masks before exiting the chamber. CBRN staff then opened additional CS capsules and poured the contents in the metal container at the rate of one capsule for every 50 recruits exiting the chamber. The next group entered and training continued in this manner until the entire BCT company completed chamber training.

Military trainers from each company provided rosters to document attendance, exposure group assignment (1-4), and mask confidence chamber completion. Recruits were included in the study population if they completed the mask confidence chamber

with their assigned BCT company. Investigators were provided a count of recruits by unit identifier and exposure group upon successful completion of the mask confidence chamber at the end of each training exercise; no personal identifying data were provided. The numbers of recruits not present for training and those from a different BCT company were listed on the rosters and excluded from the analyses. Exposure categories were assigned to each group by their CS exposure concentration: 0-0.39 mg/m^3, 0.40-1.00 mg/m^3, 1.01-1.50 mg/m^3, and greater than 1.50 mg/m^3. Exposure categories were based on ACGIH TLV-C[skin] (0.39 mg/m^3), one-half IDLH (1.00 mg/m^3) and three-fourths IDLH (1.50 mg/m^3) (4; 53).

The Occupational Safety and Health Administration (OSHA) modified NIOSH Physical and Chemistry Analytical Method (P&CAM) 304 was used to determine CS concentration for each exposure group (52; 60). Personal sampling of individual recruits was not feasible; however previous studies showed a single static sample located 26 feet from the entrance in the center of this particular chamber could characterize CS concentration during mask confidence training and be used as a surrogate for individual CS exposure (41). As with previous work, this study used a sampling train consisting of an OSHA Versatile Sampler (OVS) suspended 1.37 m above the floor (to represent the human breathing zone) connected to an air sampling pump using a 1.4 m section of Tygon tubing. The OVS contains both a filter and sorbent material, ideal for collecting both CS aerosol and vapors. The pump used was calibrated onsite to 1.5 liters per minute each day before and after sampling. The pump was started when the first recruit of an exposure group entered the chamber and stopped when the last recruit of the exposure group exited. Total sampling time was annotated from the digital readout on the

sampling pump and sample media was then capped, sealed in a plastic bag, and placed outside of the chamber in an ice filled cooler. New OVS media was then installed onto the pump and sampling continued until all exposure groups completed training.

In addition to static sampling, chamber operators were personally monitored using the same sampling train and flow rate as described above. The OVS media was clipped within six inches of the operator's nose and the pump was started when the operator entered the chamber. The pump was stopped only after the entire 200 recruit unit completed training and the operator departed the chamber. Total sampling time was annotated and samples were capped, sealed in individual bags, packaged on ice with daily area monitoring samples, and shipped within 24 hours to a certified laboratory for analysis.

Health surveillance data was captured using the same methodology described in previous work (39). Clinically diagnosed ARI case counts for each company completing the MCT were captured through existing weekly Fort Jackson Acute Respiratory Disease Surveillance (ARDS) systems (27). This surveillance program queried the Composite Healthcare Computer System (CHCS) for clinically diagnosed ARI encounters within the Fort Jackson recruit population matching one or more of the following International Classification of Diseases Version 9 (ICD-9) codes: 079.99 Viral infection, not otherwise specified (NOS); 382.9 Otitis media NOS; 460 Nasopharyngitis, acute; 461.9 Acute sinusitis; 465.8 Acute upper respiratory infections of other multiple sites; 465.9 Acute upper respiratory infections of unspecified site; 466.0 Bronchitis, acute; 486 Pneumonia, organism NOS; 487.0 Influenza with pneumonia; 487.1 Influenza with respiratory manifestation, not elsewhere classified (NEC); 487.8 Influenza with

manifestation NEC; 490 Bronchitis NOS; 784.1 Pain, Throat; and 786.2 Cough (39). Preventive medicine personnel used these data combined with military training unit specific attendance rosters to determine case and exposure group status for recruits diagnosed with ARI during their company's surveillance period. For the purposes of the present study, the surveillance period started seven days before each unit's chamber training and ended seven days after completion. Recruits who completed training with their unit and were diagnosed with ARI in the surveillance period were designated as cases. Incidence rules provided to preventive medicine personnel dictated that the first diagnosis of ARI during a surveillance period was used as the date of encounter; however if an afebrile case progressed to a febrile case later in the surveillance period, date of febrile diagnosis took precedence. A febrile case was defined as diagnosis with one or more of the aforementioned ICD-9 codes and an oral temperature greater than 100.5°C. Investigators were provided ARI count data in a format that summarized the number of incident cases by training unit, exposure group, date of medical encounter, and febrile/afebrile status. Personal identifying data were not provided to investigators (Table 6). Investigators used the date of encounter to determine if a case occurred in the week preceding the chamber (pre-chamber ARI) or in the seven days following the chamber (post-chamber ARI). Pre-chamber ARI cases were treated as non-susceptible for post-chamber ARI and were excluded from post-chamber risk calculations.

CS concentrations were matched to corresponding military unit, exposure group data, and ARI incidence and entered into SPSS Statistics for Windows (Version 19, IBM Corp., 2010) for data management. Open Source Epidemiologic Statistics for Public Health (Version 3.01, www.openepi.com., 2013) was used to calculate chi-squared

values, Breslow-Day tests for interaction, stratified risks, attributable risks, as well as unadjusted and Mantel-Haenszel adjusted risk ratios (RR) with corresponding 95% confidence intervals (95% CI). Statistical Package for the Social Sciences (SPSS) was used to calculate means, standard deviations, Shapiro-Wilk tests, and 95% confidence intervals for CS concentrations. SPSS was also used to conduct Poisson regression analyses to explore the relationship between CS exposure concentrations and ARI outcomes.

RESULTS

Exposure Assessment

Table 7 depicts the CS exposure data for trainees and chamber operators in this study. Recruit CS exposure concentrations were observed from 0.26 – 2.78 mg/m^3 ($\overline{x}$=1.04 mg/m^3) over 106 unique MCT events with exposure durations ranging from 5.0 – 25.0 minutes ($\overline{x}$=11.67 min). Personal monitoring of six chamber operators over 28 sampling episodes demonstrated CS exposure concentrations ranging from 0.05 – 2.22 mg/m^3 ($\overline{x}$=1.05 mg/m^3) with exposure durations from 20.0 – 162.0 minutes ($\overline{x}$=62.73 min). Trainee eight-hour time weighted averages (TWA) ranged from 0.004 – 0.11 mg/m^3 ($\overline{x}$=0.02 mg/m^3) and chamber operator TWA ranged from 0.02 – 0.35 mg/m^3 ($\overline{x}$=0.12 mg/m^3). Nearly 90% of area samples (n=94) and personal monitoring samples (n=24) exceeded the ACGIH TLV-C [skin] (0.39 mg/m^3); five of these (four area samples and 1 personal monitoring sample) exceeded the IDLH (2.00 mg/m^3). Neither trainees nor operators exceeded the 8-hour OSHA PEL (0.40 mg/m^3) (57).

Outcome Assessment

Of the 5,298 recruits who participated in MCT during the surveillance period, the majority (55%) completed the MCT during week two of BCT and 96% completed the training during the first three weeks of BCT (Table 8). Trainees lived in one of three building types: 1) Starship barracks (SS) – Housing units with multiple 60-person rooms; 2) Relocatable barracks (RL) – Temporary modular structures capable of housing up to 50-people per room; and 3) Star base barracks (SB) – Newer housing units with multiple 60-person rooms. Nearly half of the recruits (45%) lived in relocatable barracks. There were 155 clinically diagnosed cases of ARI (4 febrile and 151 afebrile) observed in the study population. Approximately one-third (n=56) of these cases occurred in the seven days prior to CS exposure (pre-chamber) and the remaining two-thirds (n=99) occurred during the seven days following CS exposure (post-chamber).

Table 9 shows that the overall ARI risk was significantly higher in the seven days following exposure to CS compared to the seven-day period before the exposure (RR=1.79, 95%CI=1.29, 2.47). Increased ARI risk was observed independent of the week of CS exposure or barracks building type. Stratum specific Mantel-Haenszel adjusted rate ratios did not suggest confounding and the Breslow-Day test for interaction did not suggest interaction by either variable. A chi-squared test for homogeneity revealed no significant difference between pre-chamber ARI incidence rates across chamber weeks (p=0.37), building types (p=0.38), CS concentration categories (p=0.75); or post-chamber ARI incidence rates with respect to chamber week (p=0.18) or building type (p=0.35). However, a chi-squared test for independence suggested that post-chamber ARI rates (p=0.02) were dependent upon CS exposure concentration.

A Poisson regression analysis showed a significant difference between pre and post-chamber ARI rates across all concentration categories ($p=0.049$) and significantly elevated pre/post-chamber ARI rate ratios at all concentration categories higher than the ACGIH TLV-C [skin]. These elevated rate ratios however, were not statistically different from each other ($p=0.58$) (Figure 9).

DISCUSSION

Comparing the results of this study with those conducted before ALARACT 051/2013 implementation shows that the change in Army mask confidence training procedures resulted in an approximately 10-fold decrease in the CS concentration experienced by trainees and chamber operators. It suggests implementation also resulted in a lower risk ARI diagnosis in the seven-day period following exposure to CS when compared to the seven-day period before CS exposure and further demonstrates post-exposure ARI incidence is dependent upon CS exposure concentration.

Figure 10 compares CS concentrations before and after implementation of ALARACT 051/2013 to illustrate the significant reduction ($p<0.001$) in mean CS concentrations for both groups and how these align with established exposure guidelines. This decrease resulted in fewer recruits being exposed to CS concentrations exceeding NIOSH IDLH (98% reduced to 7%), ACGIH TLV-C[skin] (100% reduced to 89%), and the OSHA PEL (12% reduced to 0%) compared to recruit exposures before implementation (41).

The reduction in CS exposure concentrations is likely due to the decrease in CS used to conduct the MCT. Prior to the recent procedural changes discussed here, MCT required the dispersal of one-650 mg CS capsule for every 30 m^3 of chamber size to

establish an initial CS concentration, followed by one additional capsule for every 10 recruits exiting the chamber to maintain the CS concentration (22; 26). ALARACT 051/2013 specified a new CS dosage formula (# of capsules = [volume (m^3)*0.0107]) that required dispersal of only 0.32 CS capsules for every 30 m^3 to establish the initial CS concentration, followed by one additional capsule for every 50 recruits exiting the chamber to maintain the CS concentration (75). This resulted in nearly two-thirds reduction in the mass of CS used to charge the chamber and an 80% reduction in the mass of CS used to maintain the CS concentration. This reduced CS mass likely resulted in the observed lower airborne CS concentrations experienced by recruits and chamber operators.

Despite chamber operators strictly adhering to the CS dosage instruction of the ALARACT, CS concentrations were not normally distributed ($p<0.001$) and ranged from 0.26 – 2.78 mg/m^3 for trainees and 0.05-2.22 mg/m^3 for chamber operators. This distribution is likely due to uncontrolled factors such as the number of times the doors of the chamber were opened and the number of times the chamber operator exited and returned to the chamber. If a recruit's mask was not properly sealed, they were asked to open the door and exit the chamber. Chamber operators often followed the recruit to ensure the mask was properly sealed before allowing chamber re-entry. This recurring scenario may have enabled aerosolized CS to escape the chamber and dilution ventilation to enter thus decreasing the CS concentration experienced by participants. During situations such as this, the personal sampling pump on the respective chamber operator was not paused, which could have also resulted in a decreased CS concentration measurement for chamber operators.

In addition to the decrease in CS concentration, recruit time required in the chamber without their protective mask was also reduced with the ALARACT. In accordance with US Army safety regulations, recruits would no longer be exposed to CS without respiratory protection beyond 15 seconds (29). Chamber operators strictly enforced this standard and unprotected exposures lasting longer than 15 seconds were not observed. In fact, nearly half of the population only removed masks for durations of less than five seconds. Even in this scenario however, recruits were still exposed via the dermal pathway for the duration of the chamber exercise.

The aforementioned changes may have contributed to the reduction in risk of post-chamber ARI diagnoses observed in this study compared with previous work. After implementation of the ALARACT, recruits had a 1.79 times greater risk of ARI diagnosis within the seven days following exposure to CS compared to the seven days before CS exposure. Similar research conducted before the ALARACT demonstrated a 2.44 times greater risk for ARI diagnosis using the same pre and post chamber surveillance periods (39). In both pre and post ALARACT studies, week of chamber training and the barracks building type did not play a significant role in ARI outcomes during the surveillance period. This contradicts previous ARI studies that demonstrated that both building type and week of training had an impact on ARI outcomes (80). Previous studies however, were conducted before mandatory adenovirus type 4 and 7 vaccine was reintroduced in this population (47). This vaccine has been shown to significantly decrease febrile ARI incidence among the BCT recruit population across Department of Defense initial military training sites (35). Observed ARI disease patterns may have changed due to the

impact of these vaccines; as such it is difficult to make comparisons of studies conducted before and after its implementation.

The lack of an observed relationship between pre-chamber ARI and CS exposure concentrations (p=0.75) coupled with pre-chamber ARI rates that were not significantly different nor elevated at any observed CS concentration levels suggested pre-chamber ARI was independent of CS exposure. Incidence of ARI after CS exposure however, was temporally linked to the exposure and was associated with CS exposure concentrations (p=0.02). Risk of being diagnosed with ARI after exposure to CS was significantly elevated in all concentrations higher than the ACGIH-TLV-C [skin] (0.39 mg/m^3). There was a statistical difference between the post-chamber ARI rate in the highest CS concentration category (>1.5 mg/m^3) compared to the lowest (0.00-0.39 mg/m^3) (p=0.02). Pre/post-chamber rate ratios were also significantly elevated in all concentrations above the ACGIH-TLV-C [skin] but were not statistically different than each other (Table 9).

The elevated post-chamber ARI rates and pre/post-chamber rate ratios at concentrations above 0.39 mg/m^3 are suggestive of a protective effect of the ACGIH-TLV-C [skin] compared to CS exposure concentrations exceeding this value. This is further supported by an observed decrease in both the post-chamber ARI rate (0.50, 95%CI=0.10, 1.54) and pre/post-chamber rate ratio (RR=0.76, 95%CI=0.17, 3.36) in this CS concentration range when compared to other groups. However, this reduction in risk was based upon only 11% (n=600) of the population and was not statistically significant. These results are consistent with previous research suggesting CS exposures below IDLH (2.00 mg/m^3) decreased ARI risk when compared to higher CS exposure concentrations (39). However, the previous study had only 2% (n=134) exposed to CS at this

concentration range making it difficult to draw conclusions regarding ARI risks at concentration gradients below IDLH. In the current study, implementation of ALARACT 051/2013 resulted in exposure of 93% (n=4,943) of the study population to CS concentrations less than 2.0 mg/m^3. This increase in sample size enabled more detailed analysis at this level and suggested a gradual reduction in elevated ARI risk as CS concentrations levels approach ACGIH-TLV-C [skin] with a potential threshold for doubling of ARI risk in the range of 0.39 – 1.00 mg/m^3. These results are also consistent with previous research suggesting a threshold effect in the range of 0.00 – 2.00 mg/m^3(39).

Table 10 illustrates the differences between ARI rates before and after implementation of ALARACT 051/2013. The overall, pre-chamber, and post-chamber ARI rates increased after implementation of the ALARACT; however only differences in pre-chamber ARI rates reached statistical significance (p=0.04). These results were expected since seasonality has been shown to be a predictor of ARI incidence in this population (71; 80). The pre-ALARACT study was conducted from August – September 2012 before the start of the cold and flu season and demonstrated a febrile ARI incidence rate of 0.030 cases/100 person-weeks and an afebrile ARI incidence rate of 1.20 cases/100 person-weeks (39). During this same period, the febrile ARI incidence rate for all trainees attending BCT at Fort Jackson, SC during this period was 0.087 cases/100-person-weeks (77). This may have resulted in lower baseline ARI incidence than the present study, which was conducted near the end of the cold and flu season with a higher febrile ARI incidence rate of 0.038 cases/100 person-weeks and an afebrile ARI incidence rate of 1.40 cases/100 person-weeks in this study population. The febrile ARI

incidence rate for all recruits attending training at Fort Jackson during this same time period was 0.091 cases/100 person-weeks (78). Despite the significantly higher baseline ARI rate observed in this study, the adjusted pre/post-chamber ARI rate ratio decreased after implementation of ALARACT 051/2013 resulting in 26.85% (95%CI=-0.17, 0.54) effectiveness for the intervention; however neither the difference in the rate ratios nor the effectiveness of the intervention achieved statistical significance (p=0.19). It still suggestive however, that this intervention may have decreased ARI risks associated with exposure to CS in this US Army BCT cohort.

This study demonstrated a lower ARI incidence rate in BCT than those presented historically, which is consistent with the study conducted before implementation of ALARACT 051/2013. This lower rate was expected due to the implementation of the Adenovirus 4 and 7 vaccines in 2011 that has been shown to significantly decrease ARI burden in this population (9; 10; 35). There were only four febrile ARI cases in the study population, one case presented before exposure to CS and the other three were diagnosed post-chamber. All post-chamber cases were exposed to CS in concentrations higher than the ACGIH TLV-C[skin]. This may suggest increased concentrations of CS increase the risk of febrile ARI; however this is difficult to determine based upon such sparse data. It also may suggest the large proportion (97%) of post-chamber cases that are afebrile in this population is respiratory irritation caused by the effects of CS rather than infection. Post-chamber ARI diagnoses due to irritation would be expected within 24 hours of MCT completion since symptoms associated with CS exposure typically resolve only minutes after cessation of exposure. However, only 5.05% of post-chamber ARI presented within 24 hours of MCT completion. In fact, only 17.17% of post-chamber ARI diagnoses

occurred within the two days following MCT. This may suggest that CS induced stress on the respiratory tract increases susceptibility to ARI causing pathogens, resulting in a higher post-chamber ARI incidence rate and more cases later in the follow-up period.

Figure 11 combines the data from the pre-ALARACT study with the results obtained in this research to cover a range of CS concentrations from 0.26 - 55.24 mg/m^3 (39). A Poisson regression analysis showed a significant difference between pre and post chamber ARI rates at all concentration levels ($p<0.001$); the risk of being diagnosed with ARI before the chamber compared to the risk of being diagnosed after the chamber was significantly elevated in all concentration categories above the ACGIH-TLV-C [skin] with the exception of 1.50 – 2.00 mg/m^3. The lack of statistical significance in this concentration category is likely due to sparseness of data as only 7% (n=836) of the combined population was exposed at these concentrations. The combined data reveal that post chamber incidence was dependent upon CS exposure concentrations ($p=0.048$) and further supports the suggestion of lower ARI risk at CS concentrations below the ACGIH TLV-C [skin] followed by an increase in risk to a threshold concentration between 0.40 and 1.00 mg/m^3 where the risk approximately doubles and remains constant. One must be cautious in interpretation of these results however as the analysis failed to detect a difference between rate ratios at the 95% confidence level ($p=0.65$).

There are several limitations associated with this observational study. Investigators were not permitted to influence the training, CS concentrations, CS exposure times, or perform any actions that had the potential to disrupt training which led to limitations in the exposure assessment portion of this study. For example, personal monitoring had the potential to disrupt training, therefore CS exposure concentrations

were based upon area sampling rather than personal monitoring. This methodology assumed that CS was evenly dispersed throughout the chamber and that all recruits within an exposure group were exposed to the same level of CS based upon one static sample. While this is an acceptable method to estimate exposures to a group of people, it does not show the variability that would be expected within a given exposure group based upon location in the chamber and number of times the door was opened (60). Furthermore, exposure time and time with mask removed often varied from recruit to recruit within exposure groups and this variability was not captured. The small amount of data in the lowest concentration category makes it difficult to determine if there is a truly a protective effect afforded by the ACGIH TLV-C [skin]. Future studies should consider reducing the amount of CS used to conduct the mask confidence chamber to lower CS exposure concentrations to better explore health outcomes related to CS exposures occurring below the ACGIH TLV-C [skin].

Another limitation lies in the inability of this study to differentiate between acute respiratory irritation and acute respiratory infection. Health outcomes were based solely upon acute respiratory related ICD-9 codes that appeared in electronic medical records, making it difficult to determine if symptoms were due to CS induced irritation of the respiratory tract or if they were the beginning of a respiratory infection. Furthermore, the brief surveillance period used here may not have been sufficient to identify afebrile cases that later progressed to febrile cases. Given this limitation, the number of febrile incident cases observed was small. In fact, the febrile rates observed in this study were lower than those observed by Army Public Health Command across the entire Fort Jackson trainee population during the study period (0.030 vs. 0.087 cases/100-person

weeks) (78). Previous studies however show that febrile ARI rates tend to peak during weeks four through six of Army BCT, and this study did not capture these data since it focused on health outcomes associated with mask confidence chamber training generally completed during the first three weeks of BCT (47; 80). Without surveillance data for each company for the entire training cycle, it is difficult to determine whether the trends observed here are due to CS exposure or are part of an underlying disease trend that peaks later in the BCT cycle.

CONCLUSION

This study demonstrated that the implementation of the controls outlined in ALARACT 051/2013 resulted in a ten-fold reduction in the CS exposure concentrations experienced by US Army recruits attending BCT at Fort Jackson, S.C. from 13 March to 30 April 2013. It also suggested this intervention may have resulted in a decreased ARI risk in the seven days following mandatory mask confidence training compared to the seven days before exposure when compared to studies conducted before ALARACT implementation. Results from the present study further supports findings from previous research that suggest the risk of ARI diagnosis after CS exposure is positively associated with CS concentration experienced by recruits.

Despite the success of this intervention in lowering CS concentrations below the IDLH, mean recruit CS concentrations still exceed the ACGIH TLV-C[skin]. As such, efforts should be made to further decrease CS concentrations since this research suggested a decreased ARI risk for CS concentrations below this level. Demonstrating the effectiveness of the military protective mask can be achieved at CS concentrations as low as the odor threshold (0.004 mg/m^3) (40). Furthermore, since CS bears a skin

notation, efforts should be made to protect exposed skin through the use of chemical protective garments during this training (4).

Future research is needed to better characterize ARI health outcomes reported here by differentiating between CS induced irritation or infection, and to explore these outcomes at CS concentrations below the ACGIH TLV-C [skin]. Research is also needed to determine if this intervention resulted in decreased hospital burden and lost training time in the BCT population.

DISCLAIMER

The views expressed in this article are those of the authors and do not reflect the official policies or positions of the Uniformed Services University of the Health Sciences, Department of the Army, Department of Defense, or the US Government.

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Table 6. Example of De-Identified ARI Health Outcome Data Provided to Investigators.

Company (UIC)	Chamber Date	Case #	Encounter Date	Febrile/Afebrile	Exposure Group
WHG01	13 Mar 2013	1	10 Mar 2013	A-Feb	1
		2	15 Mar 2013	Feb	3
		3	13 Mar2013	A-Feb	2
WHG02	14 Mar 2013	1	12 Mar 2013	A-Feb	4
		2	19 Mar 2013	A-Feb	1

Table 7. CS Exposure Concentrations for Trainees and Chamber Operators.

	N (%)	
Overall	Trainees	Chamber Operators
	5298 (100)	28 (100)
CS Concentration (mg/m^3)		
0.00 - 0.39	600 (11.33)	4 (14.29)
0.40 - 1.00	2578 (48.66)	9 (32.14)
1.01 - 1.50	1063 (20.06)	9 (32.14)
1.51 - 2.00	702 (13.25)	5 (17.86)
> 2.0	355 (6.70)	1 (3.57)

Exceeded ACGIH TLV-C (0.39 mg/m^3)
Exceeded NIOSH IDLH (2.0 mg/m^3)

Table 8. ARI Incident Cases by Week the CS Chamber Occurred and Building Type.

	N (%)		
Overall	Pre-Chamber ARI	Post-Chamber ARI	Total Population
	56 (1.06)	99 (1.87)	5298
Chamber Week			
1	9 (0.78)	17 (1.46)	1166
2	37 (1.26)	64 (2.19)	2929
3	9 (0.89)	17 (1.68)	1009
8	1(0.01)	1(0.01)	194
Building Type			
SS	21 (1.21)	39 (2.25)	1737
RL	20 (0.84)	39 (1.64)	2378
SB	15 (1.27)	21 (1.78)	1183

Table 9. ARI Rates and Attributable Risks (Per 100 person-weeks) by Chamber Week, Building Type, and CS Concentration.
($^{0\ 1}$ 95% confidence limits testing the exclusion of 0 or 1, as indicated)

ARI Rates and Attributable Risks (95% CI)				
Overall	Pre-Chamber ARI Incidence[1]	Post-Chamber ARI Incidence[1]	Attributable Risk[0]	Pre/Post Chamber Rate Ratio[1]
	1.06 (0.81, 1.37)	1.89 (1.55, 2.30)	0.83 (0.37, 1.29)	1.79 (1.29, 2.47)
Chamber Week				
1	0.77 (0.38, 1.49)	1.47 (0.90, 2.36)	0.70 (-0.16, 1.55)	1.90 (0.85, 4.25)
2	1.26 (0.91, 1.74)	2.21 (1.73, 2.82)	0.95 (0.28, 1.62)	1.75 (1.17, 2.62)
3	0.89 (0.44, 1.71)	1.70 (1.04, 2.73)	0.81 (-0.18, 1.78)	1.91 (0.85, 4.26)
8	0.52 (0.00, 3.16)	0.52 (0.00, 3.17)	0.00 (-1.43, 1.43)	1.01 (0.06, 15.95)
		Mantel-Haenszel RR		1.79 (1.29, 2.48)
		Breslow-Day Test for Interaction		p=0.97
Building Type				
SS	1.21 (0.78, 1.85)	2.27 (1.66, 3.10)	1.06 (0.19, 1.94)	1.88 (1.11, 3.18)
RL	0.84 (0.54, 1.30)	1.65 (1.21, 2.26)	0.81 (0.18, 1.45)	1.97 (1.15, 3.36)
SB	1.27 (0.75, 2.10)	1.80 (1.16, 2.75)	0.53 (-0.46, 1.52)	1.42 (0.74, 2.74)
		Mantel-Haenszel RR		1.79 (1.29, 2.47)
		Breslow-Day Test for Interaction		p=0.73
CS Concentration (mg/m^3)				
0.00 – 0.39	0.67 (0.20, 1.77)	0.50 (0.10, 1.54)	-0.16 (-1.03, 0.70)	0.76 (0.17, 3.36)
0.40 – 1.00	1.09 (0.75, 1.57)	1.77 (1.32, 2.36)	0.68 (0.03, 1.33)	1.63 (1.02, 2.60)
1.01 – 1.50	1.04 (0.56, 1.87)	2.19 (1.45, 3.28)	1.15 (0.08, 2.22)	2.11 (1.04, 4.31)
> 1.50	1.23 (0.70, 2.12)	2.68 (1.85, 3.86)	1.45 (0.27, 2.64)	2.18 (1.14, 4.19)
		Mantel-Haenszel RR		1.79 (1.29, 2.48)
		Breslow-Day Test for Interaction		p=0.57

Table 10. Comparison of Pre and Post ALARACT ARI Rates (per 100 person-weeks) and their 95% Confidence Intervals.

	Pre-ALARACT	**Post-ALARACT**	**P value**
Overall ARI Rate	2.39 (2.05, 2.78)	2.93 (2.49, 3.41)	0.07
Pre-Chamber ARI Rate	0.70 (0.52, 0.93)	1.06 (0.81, 1.37)	0.04
Post-Chamber ARI Rate	1.71 (1.42, 2.05)	1.89 (1.54, 2.29)	0.46
MH Adjusted ARI Rate Ratio	2.44 (1.74, 3.43)	1.79 (1.29, 2.48)	0.19

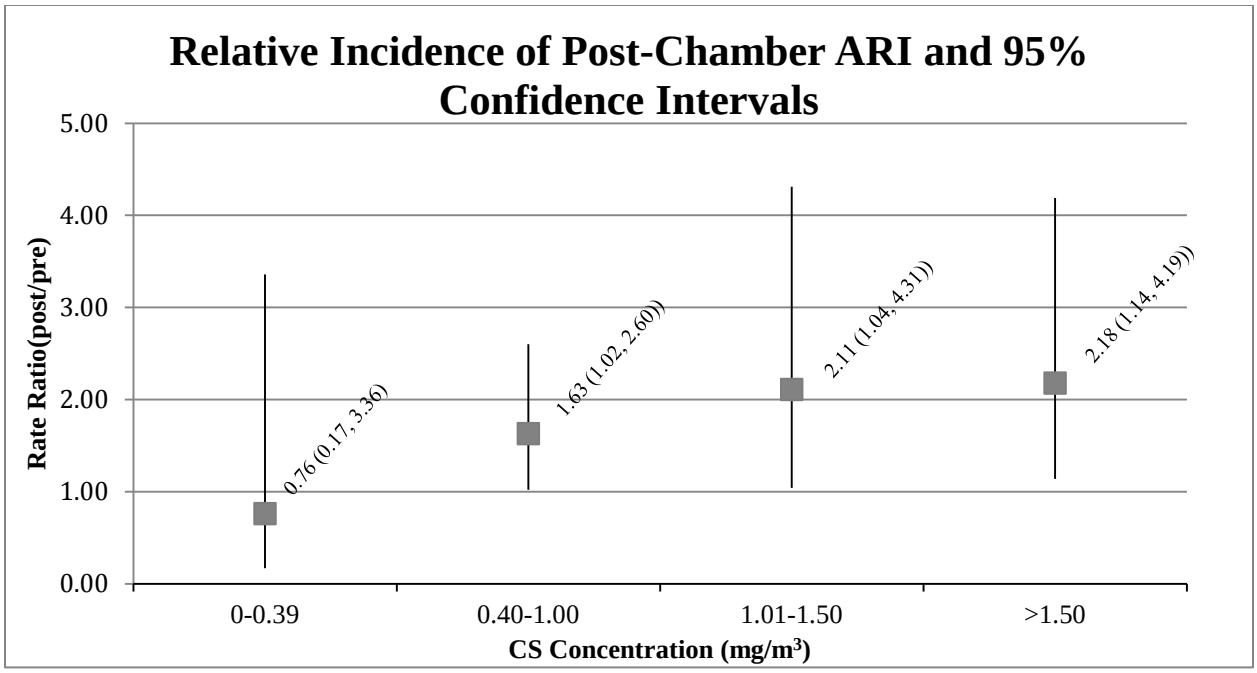

Figure 9. Relative Incidence of Post-Chamber ARI by CS Concentration and 95% Confidence Intervals.

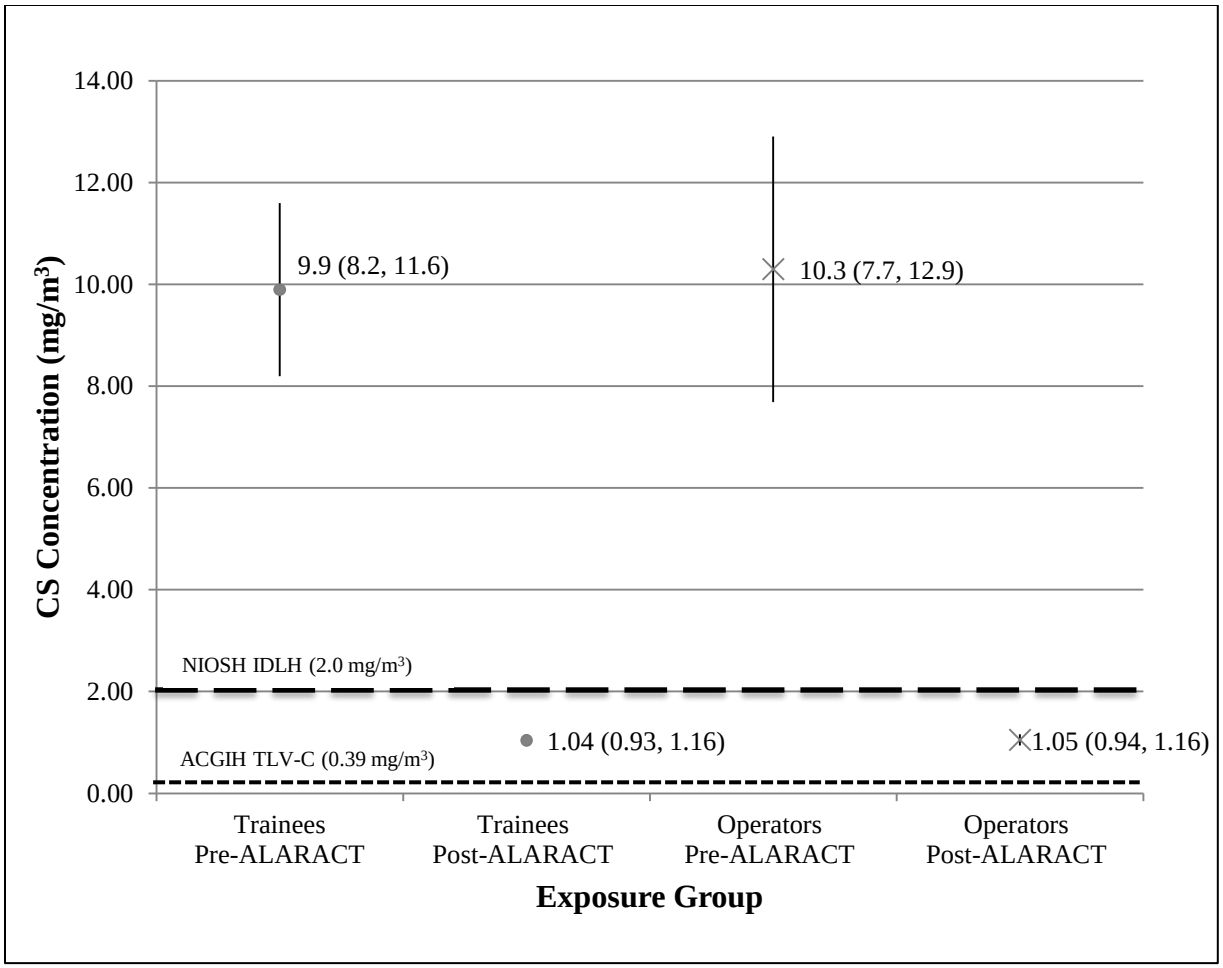

Figure 10. CS Concentration by Exposure Group, Pre and Post ALARACT.

• Represents trainee mean exposure concentration; X represents operator mean exposure concentration; vertical bars represent 95% confidence interval.

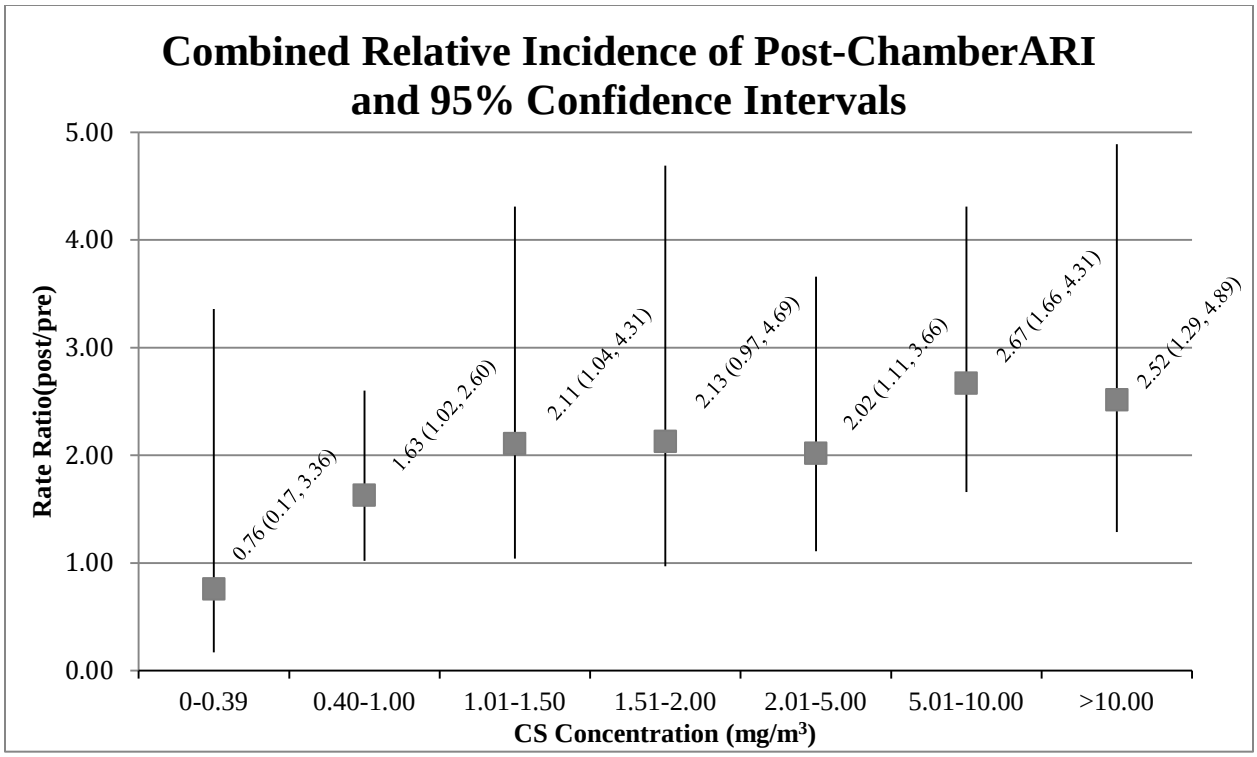

Figure 11. Combined Relative Incidence of Post-Chamber ARI by CS Concentration and 95% Confidence Intervals.

CHAPTER 7: Summary

INTRODUCTION

ARIs are the leading cause of disease burden in the world and a significant source of morbidity in US military training populations (7; 8; 11; 71; 81). ARI has been extensively studied in this population; however, causal factors are not well understood.

Research shows that ARI rates typically peak early in the BCT training cycle, followed by a decrease to baseline by completion. A 2002 study showed that ARI rates peaked during weeks four through five for febrile ARI and during week three for self-reported ARI during BCT at Fort Jackson, SC (47). A later study showed that ARI rates peaked during training weeks four through six and that the week of training is associated with both febrile and a-febrile ARI rates in an Army BCT cohort at Fort Jackson, SC (80). Several theories have been developed to explain this disease pattern including exposure to previously unencountered pathogens followed by development of immunity later in the BCT cycle and decreased immune function early in the BCT cycle due to stress and the rigors of military training events (47; 71; 80). One such event that takes place early in the BCT cycle is CS exposure during mask confidence training (26; 28).

Studies show that CS can cause significant damage to the respiratory tract in high concentrations (56; 70). Previous studies also show the potential for exposure to CS at levels considered immediately dangerous to life and health by NIOSH and potentially harmful CS thermal degradation products during US Army BCT (38; 40). An underpowered study even suggested that exposure to CS accompanied by exposure to ARI causing pathogens could pose “a significant insult to the respiratory epithelium” and promote the spread of ARI in a military population (62).

Despite evidence for exposure to potentially harmful levels of CS and CS degradation products followed by an increase in US Army BCT ARI rates after completion of MCT, no existing ARI studies considered mandatory exposure to CS in BCT as a potential risk factor for ARI diagnoses.

This research was conducted under the premise that since there is an observed increase in ARI rates following the mask confidence chamber exercise, it is possible that chemical induced epithelial damage to the respiratory tract may increase susceptibility to ARI, and thus be causally linked with subsequent increased ARI incidence rates in this population. Furthermore, the sternuatory (coughing) effects of CS may also contribute to this increased incidence by promoting transmission of ARI causing pathogens.

MANUSCRIPTS

The first manuscript quantified CS concentrations experienced by 6,723 trainees and seven chamber operators during US Army Basic Combat Training at Fort Jackson, South Carolina from 1 August to 25 September 2012. Trainee exposures ranged from 1.74 to 55.24 mg/m^3 ($\overline{x}$=9.9 mg/m^3) and chamber operator exposures ranged from 2.37 to 35.07 mg/m^3 ($\overline{x}$=10.3 mg/m^3). All 6,723 trainees were potentially exposed to CS concentrations exceeding the ACGIH TLV-C (0.39 mg/m^3), 6,589 of which were potentially exposed to IDLH concentrations (2.0 mg/m^3) specified by NIOSH. All chamber operators were exposed to concentrations exceeding both the TLV-C and the IDLH.

This initial study was important as it demonstrated the potential for CS exposures during BCT that could cause damage to the respiratory epithelium and support the hypothesis. Further, it showed that CS is approximately evenly distributed in the mask

confidence chamber at Fort Jackson, SC. It was also important from a public health standpoint as the results helped to prompt changes in MCT procedures to ensure a safer training environment for future MCT events. Specifically, the results of the initial study prompted a change in US Army policy regarding mask confidence training, dictating a reduction in the number of CS capsules required to charge the chamber, reducing the number of capsules used to maintain the CS concentration, and specifying a maximum time out of mask of 15 seconds across the entire US Army. The study also prompted policy changes requiring semi-annual industrial hygiene assessments of all Army mask confidence chambers and periodic cleaning of said chambers (75).

Our second manuscript used concentration data from the first manuscript to study the association between CS exposures and ARI related health outcomes in 6,723 US Army recruits attending BCT at Fort Jackson, South Carolina from August 1 to September 25, 2012. Recruits had a significantly higher risk (RR=2.44, 95% CI=1.74, 3.43) of being diagnosed with ARI following exposure to CS compared to the period of training preceding exposure, and incidence of ARI after CS exposure was dependent upon the CS exposure concentration (p=0.03). There was a significant pre/post exposure ARI difference across all CS concentration levels (p=0.006), however no significant differences were detected among these rate ratios (p=0.72).

This study was important as it was the first to consider CS as a covariate in ARI analyses. Since CS exposure was positively associated with ARI health outcomes in this population, interventions designed to reduce or eliminate respiratory exposures could result in decreased hospital burden, health care costs, and lost training time in the US

Army BCT population. The data provided in this analysis complemented the results from the first manuscript and resulted in the publication of ALARACT 051/2013.

Our third manuscript studied CS exposures and associated ARI health outcomes after implementation of ALARACT 051/2013 in 5298 US Army recruits attending Basic Combat Training (BCT) at Fort Jackson, SC from March 13 to April 30, 2013. It further compared these data with earlier studies to determine the effectiveness of this intervention. The ALARACT resulted in an observed 10-fold reduction ($p<0.001$) in CS exposure concentrations with recruit exposures ranging from 0.26 – 2.78 mg/m^3 ($\overline{x}$=1.04 mg/m^3) and chamber operators from 0.05 – 2.22 mg/m^3 ($\overline{x}$=1.05 mg/m^3). The overall risk of being diagnosed with ARI also decreased, but was still significantly higher in the seven days following exposure to CS compared to the seven-day period before the exposure (RR=1.79, 95%CI=1.29, 2.47) resulting in a 26.85% (95%CI=-.17, .54) effectiveness for the intervention. Post-chamber ARI rates ($p=0.02$) were still dependent upon CS exposure concentration, and pre/post-chamber ARI rate ratios were significantly elevated at all concentration categories higher than the ACGIH TLV-C (0.39 mg/m^3).

This research was the first to look at CS exposures and ARI health outcomes after implementation of ALARACT 051/2013. It supported findings from previous research that suggest the risk of ARI diagnosis after CS exposure is positively associated with CS concentration experienced by recruits and that post-exposure ARI rates are dependent upon CS exposure concentrations. It also demonstrated that CS concentrations are still above published exposure guidelines.

FUTURE RESEARCH

Future studies are needed to address the limitations associated with this research.

Studies should be conducted under an IRB approved protocol that allows for the collection of personal characteristics (e.g. body mass index, prior smoking status, sex, etc.) that have been shown to influence ARI outcomes. Efforts to better characterize ARI health outcomes reported here by differentiating between CS induced irritation or infection are also recommended. Without laboratory-confirmed pathogen specific diagnosis, CS induced injury of the respiratory tract can be misdiagnosed as infection. These health outcomes should also be explored at CS concentrations below the ACGIH TLV-C [skin]. A longer follow-up period is also recommended as the one used here may not have been long enough to observe CS induced respiratory injuries or afebrile ARI that may have progressed to febrile ARI later in the training cycle. Furthermore, a longer follow-up period would enable the investigator to observe ARI trends throughout the entire BCT cycle to identify underlying ARI trends that may influence results.

Personal air monitoring of recruits accompanied by individual time out of mask would provide a better measure for individual CS exposures. Exposure concentrations were assigned based upon an area sampling methodology which assumed that CS was evenly dispersed in the mask confidence chamber, which may not be the case under all possible exposure scenarios. Additional research is also needed to determine if implementation of ALARACT 051/2013 resulted in decreased CS concentration at other US Army BCT sites and if it resulted in decreased hospital burden and lost training time in the BCT population.

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